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BIOMEDICAL AND BEHAVIORAL SCIENCES

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CONTENTS

BIOCHEMISTRY

Use of Broth Cultures Incubated Under Stationary Conditions To Recover Escherichia Enterotoxins, Report 1: Preparations Obtained From Standard Strains of Enterotoxigenic Escherichia.....	1
Use of Broth Cultures Incubated Under Stationary Conditions To Recover Escherichia Enterotoxins, Report 2: Escherichia Preparations Isolated From Patients With Diarrhea.....	6
Synthetic Polymers as Stimulators and Extenders of Immune Effect of Protective Brucellosis Antigen .....	10
Sensitization and Hyposensitization to Bacillus Thuringiensis.....	16
Anticholinesterase Properties of Benzo[f]Quinolium Derivatives....	19
Suppression of Delayed Hypersensitivity to Sheep Erythrocytes in Flavivirus and Bunyavirus Infection: Preliminary Character- istics of Virus-Induced Delayed Hypersensitivity Suppressors....	20
Field Tests of White Amur (Ctenopharyngodon) Fry for Controlling Mosquitoes in Rice Plantation Regions .....	20
Growth and Development of New Forms of Thermus Ruber Bacteria on Media With Organic Acids.....	21

## BIOTECHNOLOGY

Use of Gas Chromatography To Analyze the Environment (1978-1980 Literature Survey) .....	22
Regulation of Insect Breeding Under Destabilizing Conditions .....	32
Effects of Low Frequency Acoustic Signals on Behavior of Pacific Herring .....	32

## ENVIRONMENT

Basic Principles of Preservation of Bodies of Water From Pollution .....	34
Microbiological Conditions and Water Quality in Lower Dnepr .....	35
Resistance of Hill Reaction to Various Damaging Agents in Two Sorts of Wheat Triticum Aestivum (Poaceae) .....	35

## MEDICINE

Development of Cooperation Between USSR and Liberated Nations in Field of Health in Light of Resolutions of 26th CPSU Congress .....	36
Inventive and Patent-Licensing Work of Moscow Scientific Research Roentgenoradiological Institute .....	43
Changes in Virulent Properties of Pathogen Strains of Zoonotic Skin Leishmania in Passage Through Phlebotomus Papatasi .....	48
Imported Ovale Malaria in RSFSR .....	49
Dysentery Amoeba Infection of Population in Southern Parts of RSFSR, Report I: Protozoological Study Data .....	49
Forensic Medical Classification of Aviation Injuries .....	50
Advisability of Comparison of Forensic Medical Expert Data on Flight Crews With Data From Onboard Recording Devices .....	50
Analysis of Fatal Car Accidents in Leningrad Oblast and Ways to Improve Medical Assistance .....	51



Health Resort Resources and Resort-Sanatorium Network in Western Siberia .....	52
Natural Therapeutic Resources of Issyk-Kul' Resort Region, Protection and Prospects of Development Thereof .....	57
Prediction of Collective Radiation Doses to AES Personnel .....	63

#### MICROBIOLOGY

Competition Between Algae in Flowing System .....	68
---	----

#### PHARMACOLOGY

Interaction of Opiates and Opioid Peptides With Brain Mediator Systems .....	69
---	----

#### PHYSIOLOGY

Neuron Mechanisms of Hypothalamus-Reticular Influence on Cerebral Cortex Activity .....	70
Dynamics of Minute Waves in Infralow Brain Activity in Various Methods of Electrical Stimulation of Two Zones in Neocortex .....	71
Spatial Hearing: Localization of Stationary and Moving Sources of Sound .....	72
Capacity for Learning and Extrapolation in Mice Selected for Different Brain Weight .....	72
Bioacoustic Characteristics of Sonar System in European Bat (Barbastella Barbastella) .....	73
Dominant and Its Significance in Animal Behavior .....	74
Nervous Regulation of Blood Liquid Status and Coagulation .....	74

#### RADIATION BIOLOGY

Attenuation of Radioprotective Effects of Acute Hypoxia on Animals Adapted to High Altitudes .....	76
Cytogenetic Analysis of Peripheral Blood Lymphocytes of Individuals Exposed to Low Doses of Ionizing Radiation .....	80

Experimental Validation of Use of Some Isothiuronium Derivatives as Radioprotective Compounds .....	85
Combined Effect of Hormones and Radioprotective Agents on Animals Exposed to Ionizing Radiation .....	91
Survival of Dogs Exposed to Lethal Doses of Gamma Radiation With Use of Chemical Radioprotective Agents Followed by Therapy..	97
Role of $\beta$ -Adrenergic Receptors in Radioprotective Effects of Isoproterenol .....	101
Biological Effects of Radiation in Chronic Hypoxia, Part 2: Specific and Nonspecific Resistance in Relation to Adaptation and Readaptation Times .....	102
Statistical Description of Effects of Single Hits With Heavy Ions of Biological Objects With Nonuniform Geometry .....	102
Reaction of Cultured Biennial Plants to Various Types of Radiation in Stages I and II of Organogenesis .....	103

#### PSYCHIATRY

Combined Sociotherapy of Mental Patients .....	104
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## BIOCHEMISTRY

UDC: 579.842.11.083.133

### USE OF BROTH CULTURES INCUBATED UNDER STATIONARY CONDITIONS TO RECOVER ESCHERICHIA ENTEROTOXINS, REPORT 1: PREPARATIONS OBTAINED FROM STANDARD STRAINS OF ENTEROTOXIGENIC ESCHERICHIA

Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 3,  
Mar 82 (manuscript received 22 Apr 81) pp 45-48

[Article by V. K. Kleganov, Leningrad Scientific Research Institute of  
Epidemiology and Microbiology imeni Pasteur]

[Text] The methods of obtaining thermolabile and thermostable enterotoxins  
(TLE and TSE) of Escherichia are time-consuming and difficult [7, 8]. We  
tried to simplify one of the described methods for recovering Escherichia  
enterotoxins.

#### Material and Methods

We recovered enterotoxins from four standard strains of enterotoxigenic E.  
coli (ETEC). As a control, we used 26 strains of enterobacteria that do  
not produce enterotoxins.

TLE and TSE preparations were obtained in the form of supernatant fluid from  
48-h broth cultures raised in flasks at 37°C under stationary (without  
shaking) conditions using a previously described method [9] with simplification  
and omission of several procedures. The cultures were incubated in Hottinger  
broth (dilution 1:2; pH 7.2-7.4), centrifuged twice, for 1 h each time, at 22-  
25°C and 8000-10,000 r/min; the supernatant was not sterilized. Supernatant  
from 18-24-h cultures incubated in the same medium [6, 9] with continuous  
shaking, which contained TLE and TSE, as well as ultrasonic lysates containing  
only TLE [5, 6], served as a control.

We demonstrated TLE in the preparations by the test of edema of the paw of a  
white mouse [1, 2] and TSE on baby mice to whom the preparations was given  
anally into the small intestine [3, 4]. A difference in mass of the right  
(experimental) and left (control) paw 48 h after administration of the material  
served as an indication of edema of the paw. A value of 65 mg or more was  
considered positive. The ratio of small intestinal mass, including contents,  
to mass of the rest of the animal's body served as the indicator of dilatation  
of suckling mouse intestine. A value of 0.091 or more was considered positive.

## Results and Discussion

Based on white mouse paw edema test, TLE appeared in the supernatant liquid of broth cultures of ETEC, cultured without shaking, in 48 h of incubation at 37°C (Table 1). TSE, in these same cultures, was demonstrated on suckling mice after 24 h. At 48 h, indices of dilatation of the animals' intestine reliably increased.

Table 1. Time of appearance of TLE and TSE in supernatant of ETEC broth cultures incubated without shaking

Incubation time at 37°C	Demonstration of TLE in paw edema test			TSE demonstration in baby mice		
	mice with edema (num) as related to total tested mice (den)	mean edema, mg	confid. interval of mean	mice with dilated intestine (num) as related to total (den)	mean dilatation paramet.	confidence interval of mean
0—5 min	0/20	16	10—22	0/6	0,062	0,058—0,066
15—30 min	0/20	14	9—19	0/6	0,066	0,062—0,072
1—2 h	0/20	21	17—25	0/6	0,074	0,069—0,079
24 h	5/25	46	39—53	6/6	0,135	0,128—0,142
48 h	20/20	164	154—174	6/6	0,154	0,148—0,160
Control broth--	0/23	10	7—13	0/10	0,024	0,020—0,028

Key: num) numerator den) denominator

Table 2. Testing of supernatant of broth cultures and ultrasonic lysates of ETEC for TLE according to mouse paw edema

Strain	Supernatant*				Ultrasonic lysates**			
	native		heated (65°C, 30min)		native		heated (65°C, 30 min)	
	a	b	a	b	a	b	a	b
ETEC (experiment):								
06:H16	14/14	142	0/5	36	8/8	252	0/14	33
015:H11	15/15	265	0/5	19	5/5	222	0/14	35
078:H11	21/21	209	0/11	38	8/8	252	0/14	36
0148:H28	15/15	193	0/5	11	5/5	264	0/10	42
Totals	65/65	197 (190—204)	0/26	23 (18—28)	26/26	246 (240—252)	0/52	32 (28—36)
NETEC (control):								
EPEC I (055 and others, 7 strains)	2/35	23	—	—	—	—	—	—
EPEC II (0124 and others, 10 strains)	0/50	13	—	—	—	—	—	—
E.coli 06:H10 (6 strains)	0/20	36	—	—	0/5	39	—	—
Totals	2/105	22 (18—26)	—	—	0/5	39 (34—43)	—	—

(Key on following page)

(Key to Table 2)

a) number of mice with edema of the paw (numerator) and number of tested mice (denominator)

b) mean parameter of edema (mg)

\*48-h cultures incubated without shaking

\*\*100-200 billion destroyed bacteria per ml preparation

Here and in Tables 3 and 4: confidence interval of the mean is given in parentheses; NETEC--nonenterotoxigenic E. coli; -) not tested.

[Translator's note: the first two letters in EPEC were not expanded in text, but could refer to enteropathogenic E. coli]

Table 3. Tests on suckling mice of supernatant from 48-h broth cultures of ETEC incubated without shaking for demonstration of TSE

Strain	Supernatant			
	native		heated (100°C, 1 h)	
	a	b	a	b
ETEC (experiment):				
06:H16	3/3	0,170	7/7	0,150
015:H11	5/5	0,157	6/6	0,130
078:H11	4/4	0,171	3/3	0,150
0148:H28	3/3	0,170	3/3	0,160
Totals	15/15	0,167 (0,161—0,174)	19/19	0,147 (0,140—0,154)
NETEC (control):				
0111:H2	1/4	0,070	—	—
028 ac	1/4	0,074	—	—
0124	0/4	0,071	—	—
S. flexneri 2a	0/4	0,057	—	—
Totals	2/16	0,068 (0,063—0,071)	—	—

Note: Here and in Table 4:

a) number of mice with dilated intestine (numerator) and number of tested mice (denominator)

b) mean parameter of intestinal dilatation

The presence of TLE in the supernatant of ETEC broth cultures incubated under stationary conditions, as well as in ultrasonic lysates of the same cultures, is confirmed by the results of testing native and heated (65°C, 30 min) preparations. Only native supernatant and ultrasonic lysates were biologically active in the edema test (Table 2). Preparations of ETEC incubated in broth under stationary conditions presented rather high biological activity, although inferior to ultrasonic lysates of the same strains in this respect. The specificity of the results was confirmed by the animals' negative reactions to administration of supernatant and ultrasonic lysates from strains that do not produce enterotoxin.

The thermostability of enterotoxin demonstrated in the supernatant from 48-h cultures incubated without shaking was confirmed by the results of testing native and heated (100°C, 1 h) preparations on suckling mice (Table 3). Although the biological activity of heated supernatant was lower than that of native supernatant, it did remain rather high. The negative results of testing control supernatant from strains that do not produce enterotoxin were indicative of the specificity of TSE demonstrated in the baby mice.

The biological activity of supernatant from 48-h cultures incubated without shaking was not inferior to the supernatant from the same ETEC incubated with continuous shaking (Table 4). No more than  $10^4$  viable bacteria remained after 2-fold centrifuging in 1 ml supernatant from 48-h broth cultures. This was not significant to demonstration of TSE. Specific results are also obtained on suckling mice when whole broth cultures are used [4].

Table 4. Demonstration of TES on suckling mice, in supernatant of ETEC broth cultures incubated with and without shaking

ETEC strains	Incubation conditions					
	stationary (48 h) experim.			shaking (18-24 h) control		
	number of exp.	results		number of exp.	results	
		a	b		a	b
06:H16	2	8/8	0,155	2	9/9	0,160
015:H11	1	4/4	0,158	1	5/5	0,167
078:H11	1	4/4	0,138	1	10/10	0,134
0148:H28	14	90/90	0,155	14	62/62	0,170
Totals	18	110/110	0,151 (0,144—0,158)	18	86/86	0,164 (0,154—0,175)

This was significant to the specificity of the results of the paw edema test on mice [2], but nonspecific reactions occurred in mice with administration of suspensions of cultures containing at least  $1 \times 10^9$  live bacteria per ml. The number of viable bacteria in supernatant of 48-h cultures incubated under stationary conditions was substantially smaller than the above minimum concentration, and it failed to elicit a noticeable nonspecific reaction in the animals. These data were indicative of the feasibility of using nonsterile preparations. In turn, it was determined that centrifuging the tested supernatants at room temperature did not lower TSE activity.

The obtained data validate the possibility of appreciably simplifying and reducing the cost of the technique for recovering a preparation containing E. coli LTE and STE.

## Conclusions

1. It was demonstrated that it is possible to obtain by a simple method a preparation of *Escherichia* containing thermolabile and thermostable enterotoxins in the form of supernatant from a 48-h culture incubated in Hottinger's broth in flasks under stationary conditions (without shaking). This preparation can be used in nonsterile form after 2-fold centrifuging of the culture, for 1 h each time, at 8000-10,000 r/min and room temperature.
2. A comparison to control preparations revealed that the obtained preparation has high biological activity and elicited specific reactions in the test for edema of the mouse paw and intrainestinal test on baby mice.

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USE OF BROTH CULTURES INCUBATED UNDER STATIONARY CONDITIONS TO RECOVER  
ESCHERICHIA ENTEROTOXINS, REPORT 2: ESCHERICHIA PREPARATIONS  
ISOLATED FROM PATIENTS WITH DIARRHEA

Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 3,  
Mar 82 (manuscript received 22 Apr 81) pp 63-66

[Article by N. I. Romanenkova and V. K. Kleganov, Leningrad Scientific Research  
Institute of Epidemiology and Microbiology imeni Pasteur]

[Text] The methods used to demonstrate the enterotoxigenicity of *E. coli*, as  
well as to recover thermolabile and thermostable enterotoxins (TLE and TSE)  
that they produce, are difficult and time-consuming [5, 6].

A modification of one of the methods of obtaining *Escherichia* TLE and TSE [7],  
which we described in our preceding article, enabled us to produce the prepara-  
tion in the form of supernatant of 48-h cultures incubated in flasks, in  
Hottinger's broth, without the usual shaking. In this study, the above-mentioned  
method of recovering enterotoxins was used for detection of enterotoxigenic *E.*  
*coli* (ETEC) among *Escherichia* isolated from feces of patients with diarrhea and  
healthy subjects.

#### Material and Methods

We examined 583 strains of *E. coli* isolated in the course of a bacteriological  
test of feces of 430 adult patients hospitalized in the same facility from  
November 1975 to February 1976, within the first days of illness, due to  
diverse acute intestinal disorders of undetermined etiology. We used as a  
control 485 *E. coli* strains isolated during a bacteriological analysis of feces  
of 242 healthy adult subjects ("decreed" and "undecreed" [verified and unveri-  
fied?]). To demonstrate enterotoxins in the preparations, we used additionally  
133 ETEC strains isolated in different years from the same number of patients  
with isolated (62 strains) and group (71 strains) intestinal diseases. Count-  
ing 4 control strains of *E. coli* 06:H10, we examined a total of 1206 *E. coli*  
strains obtained from 809 people.

We used the supernatant from 48-h cultures incubated at 37°C in Hottinger's  
broth (1:2 dilution, pH 7.2-7.4) in flasks, under stationary (without shaking)  
conditions, to determine whether the strains could produce TSE and TLE. The  
method for preparing the specimens was described in greater detail in our



Table 1.  
Incidence of demonstration of ETEC in patients with diarrhea and healthy subjects in tests on suckling pigs using supernatant from 48-h broth cultures incubated without shaking

Groups	Number of cases		Numb. of strains	
	in all	with ETEC	in all	with ETEC
Patients	430	262 (60.9)	583	262 (44.9)
Healthy subj.	242	22 (9.1)	485	23 (4.7)
P		<0.001		<0.001

Note: Percentage shown in parentheses.

0.091 or more was considered positive. The difference between mass of the right (experimental) and left (control) paw served as the parameter of paw edema 24 h after administration of the material.

## Results and Discussion

Table 1 lists the results of demonstration of ETEC in patients and healthy subjects by means of the anal test on suckling mice to test supernatant from 48-h broth cultures incubated under stationary conditions. The data are indicative of a high incidence of ETEC in the patients. The specificity of these results and correlation between isolated ETEC and diseases were confirmed by the reliably lower incidence of ETEC in healthy subjects: 9% versus 60.9% scaled to number of individuals tested and 4.7% versus 44.9% scaled to the number of examined strains (colonies).

Most of the strains capable of TSE production, which were isolated from patients and healthy subjects (205 out of 284, or 72.2%), were tested for TLE production using the edema test on the mouse paw with ultrasonic lysates (Table 2). According to data in the literature [5], ETEC strains from patients and healthy subjects that produced both enterotoxins constituted the majority--76.5% (157 out of 205). There were no differences in incidence of these variants of ETEC ( $P>0.05$ ) between strains isolated from patients and healthy subjects. The data in Table 2 confirm the enterotoxigenic nature of a significant part of the cultures demonstrated by means of testing the studied supernatants on suckling mice.

The thermostable enterotoxin contained in the supernatant of cultures incubated under stationary conditions had rather high biological activity in suckling mice, although it was less active than the TSE contained in supernatants of the same cultures incubated with shaking. We tested 49 strains referable to 6 serovars isolated from the patients (Table 3).

The results of tests for edema of the mouse paw, by means of which ultrasonic lysates of the same strains were tested concurrently, were indicative of highly active TLE in the supernatants examined (Table 4).

previous article. The supernatant of 18-24-h cultures incubated in the same medium in flasks with continuous shaking served as a control. We also used ultrasonic lysates of 24-h agar cultures [4]. Lysate of 100-200 billion destroyed bacteria was contained in 1 ml of such a preparation.

TSE was demonstrated in the preparations by the anal test on suckling mice [3] and TLE using the test for edema of the mouse paw [1, 2]. Four hours after giving the material to suckling mice, we determined the parameter of small intestinal dilatation--ratio of intestinal mass with contents to mass of the rest of the animal's body. A value of

Table 2.

Incidence of demonstration of capacity to produce TLE in test of paw edema in mice in TSE-positive ETEC strains

Group	People with ETEC (strains)	Number of str. tested for prod. of both enterotoxins	TSE+ TLE+	TSE+ TLE-
Patients	262	193 (73,7)*	147 (76,7)**	46 (23,3)
Healthy subjects	22	12 (54,5)*	10 (83,0)**	2 (17,0)
Totals	284	205 (72,2)*	157 (76,5)**	48 (23,5)

\*% of total number of cultures.

\*\*% of cultures tested for production of both forms of enterotoxin

Note: There were no differences between patients and healthy subjects ( $P > 0.05$ ) in frequency of demonstration of TSE+TLE+ and TSE+TLE- variants of ETEC

strains referable to 417 people, out of a total of 1206 E. coli strains obtained from 809 people.

Of the 148 ETEC strains isolated from patients, 113 were positive in the paw edema test with both supernatant and ultrasonic lysate. Activity of supernatant of these cultures, which was rather high per se, was lower than the activity of ultrasonic lysates. In all of the tested animals, there were consistently negative results from testing both preparations obtained from 35 strains of ETEC that produced TSE and were incapable of producing TLE. The data obtained when these strains were studied using the paw edema test did not differ from the results obtained on the same model with supernatant and ultrasonic lysate from 4 nonenterotoxigenic strains of E. coli 06:H10 isolated from healthy subjects.

Thus, the results of studying supernatant prepared by the above-described simple method enabled us to demonstrate a capacity for enterotoxin production in 418

Table 3. Biological activity of tested supernatants from 49 ETEC strains obtained from patients, according to tests on suckling mice

Cultivation conditions	Number of mice with dilated intestine (numerator) as related to number of tested mice (denominator)	Mean parameter of intestinal dilatation and its confidence interval
Stationary 48 h., (experiment)	161/203 (79.3 %)	0.116 (0.112-0.120)
With shaking, 18-24 h (control)	189/221 (85.5 %)	0.127 (0.122-0.132)

## Conclusions

1. It was shown that supernatant of 48-h cultures incubated under stationary conditions in Hottinger's broth can be used for demonstration of enterotoxigenic Escherichia in patients suffering from diarrhea. TSE (using anal test on suckling mice) and TLE (using edema test on mouse paw) could be demonstrated in the preparation.

Table 4. Demonstration of TLE in preparations studied using edema test on mouse paw

Strain group	Number of sero- vars	Number of strains	Supernatant of 48-h cultures incubated with- out shaking(exper)		Ultrasonic lysates (control)	
			a	b	a	b
ETEC TSE+ LTE+	10	113	528/547 (96.5 %)	129 (119-139)	484/488 (99.2 %)	158 (147-169)
ETEC TSE+ LTE-	5	35	0/150	21 (18-25)	0/168	29 (25-33)
NETEC E. coli 06:H10 (control)	1	4	0/20	31 (20-42)	0/19	43 (38-48)

Key: a) number of mice with edema of the paw (numerator) out of number of tested mice (denominator)

b) mean parameter of paw edema (mg) and its confidence intervals  
NETEC) nonenterotoxigenic E. coli

2. Use of the preparations tested provided a high incidence of ETEC demonstration in patients suffering diarrhea, which were not epidemiologically directly related to one another (60.9%).

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SYNTHETIC POLYMERS AS STIMULATORS AND EXTENDERS OF IMMUNE EFFECT  
OF PROTECTIVE BRUCELLOSIS ANTIGEN

Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 3,  
Mar 82 (manuscript received 27 May 81) pp 69-73

[Article by Ye. A. Dranovskaya and P. Ye. Ignatov, Institute of Epidemiology  
and Microbiology imeni Gamaleya, USSR Academy of Medical Sciences; All-  
Union Institute of Experimental Veterinary Science, Moscow]

[Text] The insufficient duration of immunity is, as we know, the main obstacle to extensive use of chemical vaccines, which are based on protective antigens of microorganisms. In our opinion, along with refinement of methods of isolation and purification, optimum programs and methods of administration, one of the important directions of creating intensive and longer immunity with chemical vaccines is to find safe and effective adjuvants, as well as immunostimulators of protective antigens. As for brucellosis protective antigen (BPA), as we have already reported [4], such traditional adsorbent-adjuvants as hydroxide gel and aluminum phosphate gel did not prolong the immunogenic properties of BPA.

We tested several synthetic polymers in this study as agents capable of enhancing the protective effect of BPA. Use of these agents as stimulators of protective antigen is a little-studied, but rather promising direction of modern immunology. The reports of several authors concerning stimulation of immune response with such polymers as poly-4-vinylpyridine and polyacrylic acid, by means of intensification of cooperation of T and B lymphocytes, as well as partial replacement of T lymphocyte function in cooperation with B cells [5, 6, 9, 10], served as grounds for our study. It was also interesting to study another synthetic polymer, which is widely known in medical practice, polyvinylpyrrolidone, used to prolong the therapeutic effects of some drugs [1, 8, 11] and antibiotics [2, 12].

Material and Methods

We tested the following synthetic polymers: poly-4-vinylpyridine (P-4-VP), polyvinylpyrrolidone with relative molecular mass of 40,000 and 490,000 (PVP-40 and PVP-490), as well as a new polymer complex, PVK. These polymers were synthesized in the blood substitute laboratory of the All-Union Scientific Research Institute of Technology of Blood Substitutes and Hormones.

Guinea pigs weighing 300-350 g were inoculated once with an antigen-polymer complex, which was prepared by mixing BPA in polymer solution of the appropriate concentration (based on 600 µg BPA/0.5 ml polymer solution of different concentrations). The mixture was allowed to stand at room temperature or in the incubator for 2 h for sorption. After this time, the antigen-polymer complex was given to guinea pigs in a volume of 0.5 ml. We examined the dynamics of antibody production in guinea pigs (after 7, 15 and 30 days, 2, 3, 4 and 6 months), using the following serological reactions: agglutination (RA), passive hemagglutination (RPHA) and Coombs' test (CT). Allergic studies were conducted using the intracutaneous test with brucellin on the 15th and 30th postinoculation days. We tested immunity of guinea pigs by means of experimental infection with a virulent culture of different species of brucellae at different post-vaccination times. One month after infection, the animals were submitted to bacteriological studies by means of cultures of different organs and tissues on solid and liquid nutrient media. Demonstration of brucellae served as the main criterion of presence or absence of immunity.

## Results and Discussion

The stimulating activity of synthetic polymers was tested on 45 guinea pigs, which were inoculated with BPA in a complex with different polymers in different doses (Table 1). We examined local and systemic reactions on the first days after administration of the antigen-polymer complex. A marked systemic reaction, in the form of severe depression, was observed after intramuscular injection of BPA together with PVK and P-4-VP. Puffiness at the injection site was tender to palpation and resorbed only on the 8th-12th day after administration of the complex. The complex of BPA with PVP did not present such marked reactogenicity: at the injection site there was some puffiness, which was not tender to palpation and resorbed completely on the 3d-5th day. No systemic reactions to the inoculation were demonstrable.

Table 1. Antibody production and bacteriological test results on guinea pigs inoculated with BPA with synthetic polymers

Group	Number of guinea pigs	Polymer	Polymer dosage, mg	RA, in IU			After necropsy		Immune animals, %	Infectivity index, % $\pm$ m
				day			were infected	were not infect.		
				7	15	30				
I	5	BPA + PVK	10	112	116	84	4	1	20	17,8 $\pm$ 3,9
II	4	Same	45	270	110	80	2	2	50	8,3 $\pm$ 7,9
III	5	BPA + PVP-40	20	128	130	96	3	2	40	15,5 $\pm$ 7,9
IV	5	Same	45	104	104	64	—	5	100	—
V	5	BPA + PVP-490	20	128	148	88	3	2	40	13,9 $\pm$ 4,4
VI	5	Same	45	120	128	148	2	3	60	4,4 $\pm$ 1,9
VII	5	BPA + P-4-VP	20	80	132	70	4	1	20	26,6 $\pm$ 5,0
VIII	5	BPA	—	120	144	34	4	1	20	35,5 $\pm$ 8,2

Intracutaneous allergy tests made 15 and 30 days after inoculation revealed that the antigen-polymer complexes used had no sensitizing properties.

Studies of dynamics of agglutinin production with the RA 7, 15 and 30 days after inoculation revealed (see Table 1) that RA titers rose by the 15th day in all animals (except group II), with a decline thereafter (with the exception of group VI). The findings indicate that the dynamics of agglutinin production in response to the antigen-polymer complex are similar to antibody production after giving BPA alone. However, there was a relatively high agglutinin level, which had a tendency to rise, in the group of animals inoculated with the complex of BPA with PVP-40, on the 30th day after administration.

Table 2. Results of serological tests on guinea pigs immunized with BPA and PVP (40,000 and 490,000) in different concentrations

Sero- logic. reac- tion	Polymer	Poly- mer con- centr. mg/dose	Geometric mean of titer at different times after inoculation						
			days			months			
			7	15	30	2	3	4	6
RA	PVP-40	100	48*	128	40	—	—	—	—
	PVP-490	100	64	128	36	—	—	—	—
	PVP-40	200	80	104	16	—	—	—	—
CT	PVP-40	100	56	352	128	140	40	140	80
	PVP-490	100	48	320	96	80	33	120	90
	PVP-40	200	72	352	120	100	23	140	55
RPHA	PVP-40	100	70	68	15	15	—	—	15
	PVP-490	100	—	16	24	—	—	—	15
	PVP-40	200	16	56	12	—	—	—	—

\*Reciprocal of titer geometric mean

Table 3. Results of testing immunogenicity of antigen-polymer complexes (BPA with PVP-40 and with PVP-490) 4 and 6 months after administration to guinea pigs

Material used for inoculation	Polymer concentration, mg/dose	Number of guinea pigs			Immune animals, %	Infectivity index, % $\pm$ m
		in expe- riment	infec- ted	immune		
BPA + PVP-40	100	$\frac{7}{8}$	$\frac{5}{7}$	$\frac{2}{1}$	$\frac{28,7}{12,5}$	$\frac{27,4 \pm 6,8}{29,0 \pm 8,8}$
	200	$\frac{8}{9}$	$\frac{4}{7}$	$\frac{4}{2}$	$\frac{50,0}{22,0}$	$\frac{19,0 \pm 9,2}{34,4 \pm 8,9}$
BPA + PVP-490	100	$\frac{10}{9}$	$\frac{4}{5}$	$\frac{6}{4}$	$\frac{60,0}{38,4}$	$\frac{13,0 \pm 6,6}{20,0 \pm 5,9}$
BPA	—	$\frac{8}{8}$	$\frac{5}{5}$	$\frac{3}{3}$	$\frac{37,5}{37,5}$	$\frac{22,2 \pm 7,3}{35,7 \pm 7,2}$
Not inoculated (control)	—	$\frac{5}{5}$	$\frac{5}{5}$	—	—	$\frac{58,0 \pm 3,8}{62,5 \pm 2,7}$

Note: Numerator--after 4 months, denominator--after 6 months.

To check the immunogenic effects of BPA complexes with polymers, the guinea pigs were infected with a highly virulent culture of Br. abortus 54, in a dosage of 50 microbial cells, 30 days after vaccination, and necropsy performed 1 month later. Such a high infective dosage was used to demonstrate the difference in capacity of the tested polymers to stimulate immunity induced by BPA. The results of testing immunity (see Table 1) revealed that there was the highest percentage of immune animals (100%) in the group given BPA together with PVP-40 in a dosage of 45 mg (group IV). PVP-490, in a dosage of 45 mg (group VI), had a less stimulating effect. All the other polymers had a very insignificant effect or did not enhance at all the immunogenicity of BPA (groups I and VII).

On the basis of our findings, we then tested the stimulating effect of PVP-40 on antibody production and immunogenic properties of BPA. We used Br. melitensis 565 in a dosage of 20 microbial cells as infection culture. Guinea pigs were given BPA in a dosage of 0.5 ml, containing 600 µg antigen and 50 or 100 mg PVP-40 (first two groups of animals, respectively). A third group was inoculated only with BPA and the fourth was not vaccinated (infection control). We kept records of serological reactions for 3 months, after which the guinea pigs were infected and, one month later, submitted to necropsy to check immunity. It was established that the titers in the RA did not differ from one another in the first 2 groups (1:130 and 1:140 after 15 days; 1:110 and 1:100 after 30 days; 1:27 and 1:16 after 2 months, with no agglutinins demonstrable thereafter). Seven out of 10 guinea pigs inoculated with BPA and polymer PVP-40 in a concentration of 50 mg and 6 out of 8 inoculated with BPA and 100 mg PVP-40 were not infected 3 months after vaccination. In this experiment, 5 out of 6 guinea pigs inoculated with BPA alone did not get infected.

Our results revealed that an increase in dosage of PVP-40 did not enhance or prolong antibody production and immunogenic properties of BPA 3 months after inoculation, which could be related to rapid elimination of the polymer. For this reason, we decided to retard its elimination by increasing the dosage and molecular mass of the polymer [3, 7, 13]. Guinea pigs were inoculated with complexes of BPA and PVP-40 in doses of 100 and 200 mg, as well as PVP with molecular mass of 490,000 (PVP-490) in a dosage of 100 mg. The results of serological tests over a 6-month period on guinea pigs inoculated with BPA and PVP-40 and PVP-490 in different concentrations revealed (Table 2) that agglutinins disappeared by the 2d postinoculation month in those inoculated with a complex of BPA and PVP, regardless of the latter's dose and molecular mass; hemagglutinin titers in the RPHA were lower than agglutinins in the RA, and they also virtually disappeared by the 2d month. Incomplete antibodies were demonstrable in the Coombs test at all tested times, with the maximum titer (1:352) demonstrable on the 15th day and a rather high level 6 months after inoculation (1:55-1:90). We failed to demonstrate distinct differences in dynamics and level of antibody production as a function of concentration or molecular mass of PVP.

The Byurne intracutaneous allergy test was negative after 24 and 48 h, 3 months after inoculation of guinea pigs. This confirmed the data we obtained previously, to the effect that the tested antigen-polymer complexes had no sensitizing properties. We also failed to demonstrate marked local or systemic reactions.

The results of testing long-term immunity--after 4 and 6 months--revealed (Table 3) that the antigen-polymer complex of BPA with PVP-490 in a dosage of 100 mg provided immunity of more guinea pigs (60%) 4 months after inoculation than BPA with PVP-40 in doses of 100 and 200 mg--28.7 and 50% of the animals, respectively. At this time, immunity persisted in 42.8% of the animals immunized only with BPA. We failed to demonstrate a beneficial effect with the use of PVP-490 and, particularly, PVP-40 6 months after inoculation (immune animals constituted 12.5 and 38.8%, respectively, with these polymers; see Table 3).

Thus, our studies revealed that, of the synthetic polymers studied, PVP stimulates the most actively the immunogenic effect of brucellosis protective antigen. PVP with high molecular mass (490,000) had a longer stimulating and prolonging effect on immunogenic properties of BPA than PVP with molecular mass of 40,000, which is apparently related to its slower elimination.

It is necessary to continue work on selection of dosage and molecular mass of PVP or other immunostimulators in order to solve the problem of designing an antigen-polymer complex based on BPA for longer stimulation of its effects. It is also necessary to work out optimum modes of interaction between BPA and polymer molecules to obtain a more stable compound.

#### Conclusions

1. The dynamics of antibody synthesis after giving guinea pigs a complex of BPA and PVP or other synthetic polymers do not differ from the dynamics of antibody production when animals are immunized with BPA alone.
2. Intramuscular injection of BPA in a complex with PVP does not have a sensitizing effect, does not elicit marked local or systemic reactions.
3. PVP with molecular mass of 40,000 has a stimulating effect on immunogenic properties of BPA, enhancing intensity of immunity; however, its effect was brief; PVP with higher molecular mass (490,000) stimulates the protective properties of BPA for a longer time, and this is apparently related to its slower elimination.

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SENSITIZATION AND HYPOSENSITIZATION TO BACILLUS THURINGIENSIS

Moscow GIGIYENA TRUDA I PROFESSIONAL'NYYE ZABOLEVANIYA in Russian No 10, Oct 81  
(manuscript received 26 Mar 81) pp 53-54

[Article by L. P. Shuvalov, N. D. Golidonova, V. N. Drozdov and V. P. Padalkin  
(Moscow), All-Union "VNIIBiotekhnika" Scientific Research Institute of  
Bioengineering]

[Text] Bacterial insecticides based on *B. thuringiensis*, live spores and toxins are being used with success to control insects that damage agricultural crops. According to a number of authors (E. K. Afrikyan; Ya. Veyzer), bacterial insecticides based on *B. thuringiensis* are harmless to warm-blood animals and man. However, other researchers (S. A. Ivashina; L. I. Izraylet and R. Ye. Kogay) report that such agents may have a deleterious effect on man, causing various allergic diseases. For this reason, problems arise that are related to desensitizing individuals who are allergic to this microorganism.

It has been established that ascorbic acid has an antiallergic effect, the mechanism of which is related to its effect on the pituitary-adrenal cortex system (B. L. Smolyanskiy). Several authors (V. I. Pevzner; Ye. Martini) indicate that ascorbic acid is capable of normalizing vasotissular permeability. Its role is known in raising the titer of enzymes involved in inactivation of biologically active substances (B. N. Gol'dshteyn; Ye. V. Rayka). Because of its desensitizing properties, ascorbic acid is used extensively in the treatment and prevention of various allergic diseases.

Our objective here was to make an experimental study on guinea pigs of the possibility of producing heightened sensitivity of the delayed type to *B. thuringiensis*, as well as using ascorbic acid to desensitize these animals.

The studies were conducted on male guinea pigs weighing 300 g. The animals were divided into 4 groups, with 12 animals in each group. The first group of guinea pigs was given hypodermic injections of live vegetative culture of *B. thuringiensis* var. *galleriae* twice at an interval of 30 days, in doses of 1 billion cells; the second group was given a spore culture under the same conditions. The third group was given 2 mg ascorbic acid for 20 days, per os, 10 days after the last injection of spore culture. The control group consisted of intact animals.

To obtain leukocytes, 10 ml blood was taken from the heart 30 days after the last injection. Cells were isolated by adding 1 ml 10% gelatin to heparinized blood.

The reaction of inhibition of leukocyte migration was run in capillaries, which contained nutrient medium No 199 with 10% bovine serum (George and Vaughan), placed in a chamber.

We used entobacterin as specific antigen; it is a nitrogen-containing polysaccharide obtained from a culture of *B. thuringiensis* var. *galleriae* by extracting antigenic material in an alkaline medium at elevated temperature and pressure. The sterile, lyophilized preparation of antigen contained up to 10% protein, 52% polysaccharides and up to 30% nucleic acids. For inhibition of leukocyte migration, antigen was put into the nutrient medium in a dosage of 0.02 mg/ml. This dosage does not elicit degenerative changes in the cell culture (S. A. Dzharlygasov et al.).

It was established that the specific antigen, entobacterin, elicited inhibition of leukocyte migration in guinea pigs immunized with a culture of *B. thuringiensis* (both sporulated and vegetative forms). With immunization using the vegetative form, the average percentage of inhibition constituted  $56.4 \pm 9.08$  and with the sporulated form it was  $65.7 \pm 11.35$ . However, the difference in immune response was statistically unreliable ( $P > 0.5$ ).

In control (intact) animals, the mean inhibition of leukocyte migration constituted  $10.37 \pm 4.59\%$ , which is substantially lower than in the first and second groups of animals ( $P < 0.001$ ).

In the course of immunization with a sporulated culture of *B. thuringiensis*, the third group of guinea pigs received ascorbic acid; average inhibition of leukocyte migration did not differ from the control and constituted  $11.02 \pm 3.78\%$ . In the group of animals who were not given ascorbic acid this parameter constituted  $61 \pm 7.2\%$ .

The difference in inhibition of leukocyte migration between sensitized and desensitized guinea pigs was statistically reliable ( $P < 0.001$ ).

Thus, subcutaneous immunization of guinea pigs with *B. thuringiensis* elicited development of heightened sensitivity of the delayed type, which was demonstrable in the reaction of inhibition of leukocyte migration in response to the specific antigen, entobacterin. Ascorbic acid inhibited development of sensitization to *B. thuringiensis*.

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10,657

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ANTICHOLINESTERASE PROPERTIES OF BENZO[f]QUINOLIUM DERIVATIVES

Moscow BIOKHIMIYA in Russian Vol 46, No 10, Oct 81  
(manuscript received 17 Sep 80) pp 1764-1767

KULESHOV, V. I., KOZLOV, N. S., LIBMAN, N. M., KOSMACHEVA, I. M.,  
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[Abstract] The importance of quinoline derivatives in plant physiology and their antimicrobial properties, and the recognition that benzo[f]quinolium (BQ) derivatives are potent inhibitors of cholinesterase (ChE), led to the testing of previously unstudied ethyl-p-toluenesulfonate derivatives of 1-methyl-(ethyl)-3-aryl-BQ for their effects on equine blood butyryl-ChE (BChE) and human blood acetyl-ChE (AChE). These derivatives were established to function as mixed-type (competitive-noncompetitive) reversible inhibitors with inhibition constants ( $K_i$ ) of  $2.20 \pm 0.49 \mu\text{M}$  for AChE and  $9.43 \pm 0.39 \mu\text{M}$  for BChE. Evaluation of the inhibitor-AChE interaction indicated that hydrophobic binding was the key step which promoted the interaction of the para-substituent on the phenyl ring with negatively charged sites outside of the active site. Figures 3; references 10: 4 Western, 1 Belorussian, 5 Russian.  
[158-12172]

SUPPRESSION OF DELAYED HYPERSENSITIVITY TO SHEEP ERYTHROCYTES IN FLAVIVIRUS AND BUNYAVIRUS INFECTION: PRELIMINARY CHARACTERISTICS OF VIRUS-INDUCED DELAYED HYPERSENSITIVITY SUPPRESSORS

Moscow IMMUNOLOGIYA in Russian No 5, Sep-Oct 81  
(manuscript received 17 Mar 81) pp 35-37

LIPOVKA, V. A., KHOZINSKIY, V. V. and SEMENOV, B. F., Institute of Poliomyelitis and Viral Encephalitides, USSR Academy of Medical Sciences, Moscow

[Abstract] Partial suppression of hypersensitivity of a delayed type to sheep erythrocytes, ( $HDT_{SE}$ ) was seen in mice with a symptom-free infection evoked by Tachynia virus and acute lethal tick encephalitis. This  $HDT_{SE}$  was not seen after injection of attenuated yellow fever virus. This virus-induced immunological defect is attributed to activation of non-specific cell-suppressors which appeared temporarily in splenocytes, thymocytes and lymphocytes of the infected animals. Figures 4, references 7: 4 Russian, 3 English.

[142-12131]

UDC 614.449.57:576.895.711:591.617:597

FIELD TESTS OF WHITE AMUR (CTENOPHARYNGODON) FRY FOR CONTROLLING MOSQUITOES IN RICE PLANTATION REGIONS

Moscow MEDITSINSKAYA PARAZITOLOGIYA I PARAZITARNYYE BOLEZNI in Russian Vol 50, No 6, Nov-Dec 81 (manuscript received 21 Jul 80) pp 75-78

SHUMKOV, M. A., MOTENKOV, Yu. M., STARCHIKOV, A. V. (deceased) and SHILENKO, Yu. V., Rostov Scientific Research Institute for Medical Parasitology, RSFSR Ministry of Health, All-Union Scientific Research Institute for Rice

[Abstract] As a biological method for controlling Anopheles maculipennis at the preimaginal stage, fry of the cold-water white amur were introduced into rice fields of the Krasnoye farm in the Krasnodar Kray in mid-June; from 15,000- to 50,000 fry per hectare were released. In tests at 15-20,000 fry/hectare, nearly 70% of mosquito pupae were destroyed; with 50,000 fry/hectare, 91.1% were eliminated. Further effects included elimination of weeds, leading to higher rice yields, and significant fish harvests. Herbicide and insecticide use was eliminated, thus reducing environmental pollution. References: 16 Russian.

[139-12131]

GROWTH AND DEVELOPMENT OF NEW FORMS OF THERMUS RUBER BACTERIA ON MEDIA WITH ORGANIC ACIDS

Alma-Ata VESTNIK AKADEMII NAUK KAZAKHSKOY SSR in Russian No 3, Mar 82  
pp 66-67

TULEMISOVA, K. A., USERBAYEVA, G. B. and MAMONOVA, L. P.

[Abstract] Studies were conducted on the growth characteristics of new forms of the obligate thermophilic bacteria *Thermus ruber*, isolated from hot springs in southern Kazakhstan. Cultivation of the strains at 55°C on media with different sources of carbon demonstrated that the rate of growth and final biomass accumulation were far superior on organic acid-containing media than on a lactose media, particularly on media supplemented with acetic, oxalic, or pyruvic acid which gave biomass yields 1.4-1.5 times greater than the lactose medium. Superior growth on organic acids was ascribed to their greater state of oxidation, which facilitated their assimilation at high temperature when oxygen solubility in the medium is decreased. Figures 1; references 4 Russian. [254-12172]

## BIOTECHNOLOGY

UDC: 614.7:543.544(048.8)

### USE OF GAS CHROMATOGRAPHY TO ANALYZE THE ENVIRONMENT (1978-1980 LITERATURE SURVEY)

Moscow GIGIYENA TRUDA I PROFESSIONAL'NYYE ZABOLEVANIYA in Russian No 10, Oct 81 (manuscript received 15 Apr 81) pp 35-40

[Article by S. F. Yavorovskaya (Moscow), Institute of Industrial Hygiene and Occupational Diseases, USSR Academy of Medical Sciences]

[Text] The main purpose of studying the environment is to benefit mankind. Monitoring of pollution of environmental objects has been set up in our country and abroad. The main objects monitored are air and water--inland and in the seas. This task can be done the most thoroughly by using gas chromatography, and one should include among its advantages the relatively low levels that can be detected, high degree of selectivity and feasibility of analysis of multicomponent mixtures.

Gas chromatography of impurities occupies a prominent place in books by Soviet and foreign authors: G. I. Aranovich et al., V. G. Berezkin, A. V. Kiselev, and Ya. I. Yashin, M. S. Kleshcheva et al., M. D. Manita et al., R. Grob, V. Leyte. There are several surveys dealing with this matter: analysis of air--N. Sh. Vol'berg and I. I. Pochina, Yu. S. Drugov and V. G. Berezkin, B. V. Ioffe et al., A. N. Korol' and L. S. Lysyuk, B. A. Rudenko and G. I. Smirnova, S. F. Yavorovskaya, Yu. S. Drugov, Lamb et al.; analysis of water--S. F. Yavorovskaya and B. I. Anvayer, Drozd and Novak, Fishman and Erdmann, Koch, Kubilka et al.

There is a section on analysis of the environment in the survey of Soviet works on gas chromatography by A. A. Zhukhovitskiy.

There are many articles by Soviet and foreign authors dealing with analysis of air. Of interest is the one by A. V. Garusov et al. concerning the use of water as the labile phase in analyzing homologues. V. D. Yablochkin collected samples in vaseline oil, heating 3 ml thereof in a desorber and analyzing 3 ml of the vapor-gas phase to assay volatile substances. A. G. Vitenberg and I. A. Tsibul'skaya proposed a new variant for the method of equiponderant concentration: the sample was placed in 2 ml 80% acetic acid, the solution was transferred into a syringe containing 2 ml 40% caustic potash [potassium hydroxide] and chromatographed the gas phase. M. T. Dmitriyev et al. assayed hydrocarbons, aromatic compounds, aldehydes, alcohols and other impurities, collecting samples on tenax adsorbent. Thorburn and Colenutt concentrated



volatile organic compounds on activated carbon and extracted carbon disulfide. There was 99% extraction. Many works by Soviet and foreign authors deal with analysis of atmospheric and industrial air. B. V. Ayvazov et al. assayed acetone, benzene and its homologues in the atmosphere of industrial enterprises, using 15% PEG-20M [polyethylene glycol] on chromaton [?] as the stationary phase. The sensitivity threshold is below the MPC [maximum permissible concentration] of the components. Analysis of a mixture consisting of styrene, acrylonitrile, benzene and other substances that pollute the industrial environment was made by M. D. Babin on columns with apiezon and "kabavaks" [typo for carbowax?]. Determination was made of concentrations below the MPC. Accumulation was required for acrylonitrile.

L. D. Pribytkov analyzed atmospheric air for styrene in the presence of paraffin and aromatic hydrocarbons. L. Ya. Rubinskiy et al. (1978) assayed total amounts of nonaromatic hydrocarbons, also in atmospheric air, using tripropionitrilamine as the stationary phase.

Mackay and Hussein used a large diameter (4.7 mm) capillary column with SE-30 stationary phase to concentrate volatile organic compounds. Analysis was made on Carbowax-20M raising the temperature from 70 to 230°C. Trace amounts of hydrocarbons were assayed by Schneider and Brudekker, as well as Ulrich and Seifert.

Samples were collected in tubes filled with tenax and cooled with liquid nitrogen. Range of detection constituted  $2 \cdot 10^{-3}$  mg/m<sup>3</sup>.

Separate assays of gasoline and benzene fumes in air were made by Krajewski and Nowicka using the Mepa-Elmat Polish chromatograph. The method enabled them to detect 250 mg/m<sup>3</sup> air extraction gasoline and 15 mg benzene. Hlavay and Gullbault assayed ammonia in ambient air using a piezoelectric detector, the working element of which was coated with glutamic acid. Other substances present in 100- and 1000-fold excess did not hinder the assay. A refined method of gas chromatography was used by Pumpeng et al. to assay nitrogen oxide in the field. Samples were collected in molecular 13X screens activated by heating in vacuum at 350°C for 24 h. The analysis temperature was programmed at 40 to 210°C. Nitrogen oxide was detected at 180°C. I. A. Pinigina and V. V. Zyкова assayed hydrogen sulfide (0.03 mg/m<sup>3</sup>) and sulfuric gas (0.1 mg/m<sup>3</sup>) using a detector according to electron capture, in the presence of hydrogen sulfide. Small amounts of hydrogen chloride were detected in the stratosphere by Bachman et al., who used a capillary column with OU-17, electron-capture detector and temperature programming from 100 to 180°C.

Many works deal with carbon monoxide. Thus, A. L. Pertsovskiy et al. (1978) detected carbon monoxide in atmospheric air after conversion to methane, with analysis of the latter in an ionization-flame detector. The range of detection is 0.05-0.1 mg/m<sup>3</sup>. L. Ya. Ruvinskiy et al. (1979) used the reaction-chromatography method: carbon monoxide on a nickel catalyst was converted to methane and analyzed with a flame-ionization detector. V. G. Guglya used a thermochemical piezoelectric detector to demonstrate  $2.5 \cdot 10^{-1}$  mg/m<sup>3</sup> carbon monoxide in the presence of hydrogen and ethylene. Popp and Oppermann used an argon ionization detector and glass column, 100x0.3 cm in size, filled with molecular 5A screens. In a 250-ml air sample, they found 0.4 mg/m<sup>3</sup> carbon

monoxide. Romano and Renner converted ethylene oxide to ethylene glycol for detection, using 0.1 N sulfuric acid for absorption. Analysis conditions: stationary phase Igepal SO-990, temperature 160°C and flame-ionization detector. G. S. Pavlovskaya et al. examined the products of oxidation destruction of axle oil, lubricants and coolants at 480-500°C. Carbon monoxide was detected, as well as aliphatic and aromatic hydrocarbons.

There is a considerable number of studies dealing with oxygen-containing substances. L. I. Rapoport et al. detected acrylates in work zone air. The demonstrated amounts of methyl acrylate constituted 0.10-0.93 mg/m<sup>3</sup>. Oazi and Vinceni developed conditions for detection of acetic anhydride in the presence of acetic and formic acids and methyl acetate. Wathne assayed maleic, fumaric and succinic acids on the basis of their methyl ethers: pentane extract was analyzed at programmed temperatures of 70 to 240°C. Phenol, furfural and furfuryl alcohol were assayed by V. V. Tarasov et al., in a study of the composition of volatile products under simulated conditions. M. T. Dmitriyev et al. developed a method for detecting methanol in the presence of fumes of gasoline and benzomethanol fuel. The minimum demonstrable concentrations of methanol constituted 0.2-0.3 mg/m<sup>3</sup>. Traces of aldehydes and ketones were detected by Smith and Drummond on the basis of their dinitrophenyl hydrazones using a Hewlett-Packard 5840A chromatograph, raising column temperature to 250°C. The minimum demonstrable amount constituted 10 µg/ml.

A considerable number of works have been published on analysis of haloid-containing compounds. Epichlorohydrin was detected in the presence of furfural, acetone and furfuryl alcohol by R. S. Kamalov, with sensitivity of 0.1 mg/m<sup>3</sup>. Chlorohydrocarbons were the object of the studies of Yu. S. Drugov and G. V. Murav'yeva, Burghardt et al., Mann et al., Langhorst et al. Methods were developed for detection of vinyl chloride and 1,2-dibromomethane. Heil et al. did some interesting work on detection of C<sub>1</sub>- and C<sub>2</sub>-chloro- and fluoro-hydrocarbons in amounts of 10<sup>-9</sup> to 10<sup>-12</sup> g. Krockenberger et al. assayed vinyl chloride in a mixture of 21 organic compounds: Stationary phase--mixture of "parapak" [?] S and F.

Langhorst et al. used 1.5% potassium salt of 2,4,6-trichlorophenol on glass spheres as adsorbent to collect air samples contaminated with carcinogenic methyl ether. Sherman et al. detected ether chloride ["chloro ether"] in the environment. A method of collecting samples and analyzing polychlorinated naphthalenes was developed by Erickson et al., using a multichannel ionization detector. In samples collected for 2 days near industrial enterprises, concentrations of 150-1400 ng/m<sup>3</sup> were detected. Dobecki and Krajewski detected vinyl chloride and vinyl acetate at work places. Bruner et al. detected a complex mixture of organohalogen compounds. Samples were collected on "strong" (carbon) and "weak" (carbopak, tenax) adsorbents. Column was filled with carbopak C, with 1.0-0.1% polar phase SP 1000. Minimal demonstrable amount of freon 21 -- parts per trillion. Fuselli et al. worked on detection of organic nitrogen-containing compounds. Sensitivity of analysis of a mixture consisting of methyl, dimethyl and trimethyl amines constituted about 0.003 parts per million. Hunt et al. developed a method for detection of dinitrotoluene, collecting samples on silica gel with chloroform desorption. Sensitivity of detection with a flame-ionization detector 0.1 mg/m<sup>3</sup>. Glaser and Woodfin demonstrated 2-nitropropane collecting samples on Chromosorb 106 and analyzing them on a Packard

427 chromatograph. Shelf life of the samples was 28 days. Campbell and Moore analyzed the air of industrial buildings for acrylonitrile, acrolein, acetonitrile and acetone. Penton also analyzed acrylonitrile with sensitivity threshold of 3 mg/m<sup>3</sup>.

M. A. Klisenko and D. B. Girenko analyzed air for organophosphorus pesticides after concentration thereof, under the following conditions: stationary phase PEG-20M or SE-30, column temperature 140-185°C, thermionic or electron capture detector. N. S. Podkovyrina et al. detected DDT with concentration in heptane or oxane. Analysis of polynuclear aromatic hydrocarbons was made by Bjorseth and Eklund on a glass capillary column with stationary phase SF<sub>4</sub>54 and temperature of 100 to 250°C. The work of Radziuk et al. deals with analysis of organometal compounds, using an atom-absorption spectrometer as a detector.

There are also many works dealing with gas chromatography of water. G. A. Smol'yaninov et al. were concerned with detection of petroleum products in natural and sewage water. In addition to carbon composition and type of petroleum product, an assay was made of total quantity thereof, as well as levels of different petroleum fractions. In a sample of sewage water, 29 peaks were identified, which corresponded to hydrocarbons C<sub>8</sub>-C<sub>36</sub>. McCarthy et al. used a capillary column for analysis of potable water, with simultaneous use of a flame-ionization and electron capture detectors. The minimum demonstrable quantity constituted parts per billion in 5 ml water. Rhoades and Nulton extracted trace amounts of benzene, toluene, naphthalene, phenols and others from water using pentane or diisopropyl ether after saturating the samples with sodium chloride. Trace amounts of organic carbon on the order of 1·10<sup>-8</sup> g were detected by V. G. Rezchikov et al. after using an electric discharge on organic compounds. Drozd et al. used the RPF [expansion unknown] method for detection of hydrocarbons in parts per billion. The samples were brought up to a volume of 1 ml without flow separation and without preconcentration.

A. L. Pertsovskiy et al. used gas chromatography for detection of nitrates and nitrites (after conversion to nitrates). The nitrates were converted to nitrobenzene and analyzed on a column filled with 5% neopentyl glycol succinate on chromatone. Sensitivity of detection constituted 0.05 mg/l nitrogen. Solvents (acetone, methanol, n-butanol and others) in waste water were assayed on a column filled with polyglycerin on TND-TS-M by B. V. Aznabayev. Sensitivity of the method constitutes 0.001%. R. G. Tukmanov et al. worked on detection of fatty C<sub>2</sub>-C<sub>4</sub> acids. Moistened nitrogen served as the carrier gas. Sensitivity of analysis constituted 0.003 wt.% in a 10 μm sample of water.

G. M. Belokleytseva et al. assayed aldehydes and ketones after conversion to hydrazones. The stationary phase was chromatone + 10% E-301. Sensitivity of the method is 0.025-0.35 mg/l. N. R. Litvinov and T. M. Lyutova were concerned with plasticizers in liquid sewage. They separated a mixture of dibutyl phthalate, dibutyl sebacate and dioctyl adipate on SKTFT-50Kh silicon rubber with added neopentyl glycol succinate. Several studies of foreign authors were concerned with detection of halogen-containing hydrocarbons. Simmonds and Kerks studied the effect of input temperature on the results of analyses of a mixture consisting of chloroform, bromoform and dichloromethane, with direct input of water samples through a semipermeable membrane. Dietz

and Singley used the RPF method for detection of trichloroethylene and tetrachloroethylene in water. They analyzed 2 ml vapor on a glass column at 85°C with an electron capture detector. This method was also used in other studies: Hu and Weiner demonstrated tri- and tetrahalogen methanes, Cowen and Baynes analyzed complex mixtures of volatile toxic substances in natural and sewage water, Umbreit and Grob examined the theoretical bases and practical aspects of this method. They assayed methyl, ethyl and vinyl chlorides in water. The minimum concentration demonstrable with an electron capture detector constituted 1 µg/l in a 1-2 ml sample in the vapor phase.

The article of A. F. Shushunova et al. deals with gas chromatographic assays of diethyl and dimethyl nitrosamines in aqueous solutions and liquid sewage. The minimum demonstrable concentration in gas carrier constituted  $1.3 \cdot 10^{-8}$  and  $1.0 \cdot 10^{-8}$  mg/ml. DiCorcia et al. detected aliphatic C<sub>1</sub>-C<sub>4</sub> amines, C<sub>1</sub>-C<sub>3</sub> alcohols and acetone on graphite soot of Carbonak B modified with 0.3% KOH and 4.8% PEG-20M in water. Dinitrotoluene isomers were analyzed by Hashimoto et al. using a capillary column with apiezon L and EZD.

Polycyclic aromatic hydrocarbons were assayed by Faltusz after precipitation with magnesium hydroxide. After centrifuging, the sediment is dissolved and organic substances extracted with cyclohexane. Assays were made of 5 PAU [expansion unknown] on a glass column with stationary phase of OV-17 on a chromosorb. Considerable attention was devoted to analysis of pesticides. V. D. Chmil' et al. assayed residual amounts of 2,4-dichlorophenol on a glass column filled with chromatone N-AW-DMCS + 10% diethylene glycol succinate and 1% phosphoric acid. F. B. Girenko et al. developed methods for separate assays of residual amounts of organophosphorus pesticides. Belcher et al. used gas chromatography to assay copper and nickel in tap water after conversion to chelates. Copper levels of the order of 0.25 µg/ml were detected.

We should also mention soil analyses among Soviet works on environmental protection. As an example, we can mention assays of cumene, styrene and α-methyl styrene in the vicinity of petrochemical plants, made by R. F. Daukayeva, as well as Wood's analysis of traces of some hydrocarbons in interparticle gases of oil-bearing soil.

The foregoing material, which is far from exhaustive, indicates that gas chromatography is still being developed intensively as it applies to analysis of the environment.

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REGULATION OF INSECT BREEDING UNDER DESTABILIZING CONDITIONS

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(manuscript received 19 Jul 80) pp 31-34

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[Abstract] Evaluation was conducted on two approaches to breeding standard populations of *Culex pipiens molestus* Forsk mosquitoes: a) the method of evolutionary planning, which involves adjusting two variables (population density of the inoculum and the quantity of food per individual larva), and b) breeding under rigidly controlled conditions. Analysis of the results in terms of a desirability function ( $D \geq 0.37$ ) demonstrated that in the former case nine of the 16 experiments gave satisfactory results, versus only two out of ten in the latter case. The advantages of the evolutionary planning method lie in the continuous adjustments made in the variables which compensate for temporal biological drift. Figures 2; references: 7 Russian.

[149-12172]

UDC 597-151:639.2.081.9

EFFECTS OF LOW FREQUENCY ACOUSTIC SIGNALS ON BEHAVIOR OF PACIFIC HERRING

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[Abstract] Investigations were conducted on the use of acoustic signals to manage the Pacific herring in breeding ponds. Evaluation of the behavioral patterns of a school of herring (250 individuals) in response to 150-160 dB signals (90% 18-90 Hz) at a distance of 7 to 108 m, showed that their velocity

increased 1.5-2.2-fold and that the individuals tended to crowd together, rendering the school 1.5-3.2 times as compact. The time required for the recovery of individual and group rushes at the baseline level was inversely proportional to the distance between the school and the pneumoemitter. The results indicated that acoustic signals can be used in controlling the movement of herring under enclosed conditions. References 14: 1 Western, 13 Russian.  
[149-12172]

## ENVIRONMENT

UDC: 574.63

### BASIC PRINCIPLES OF PRESERVATION OF BODIES OF WATER FROM POLLUTION

Kiev GIDROBIOLOGICHESKIY ZHURNAL in Russian Vol 18, No 2, Mar-Apr 82  
(manuscript received 18 Jun 81) pp 48-51

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[Abstract] Studies have shown that where purified waste water from the Baikal pulp and paper combine is dumped into the bottom layers of the water there has been a restructuring of bottom biocenoses. Some species have disappeared, others have appeared. Four species of mollusks have been found in a spot with cellulose and lignin deposits, the predominant one being *Benedictia baicalensis*. Alteration of faunistic groupings is simultaneously occurring here. Representatives of general palearctic fauna are replacing Baikal endemic species of chironomid larvae. Groupings of microorganisms have also changed, with an increase in sulfate reducing, thion, methane forming and putrefactive species. All of these changes are caused by industrial wastes containing mineral salts which do not exceed the level of the established standards for protection of surface drinking water. This indicates the need to make the rules more stringent. The "rules" in practice include the body of water in the system of purification devices of enterprises as their last link. Resolution of the problem of protection of reservoirs has to take into account the unique features of each reservoir: species content, physiology and functioning of populating organisms, resistance and susceptibility of hydrobiocenoses, geographical location, volume, depth, dimensions and so on. The "rules" ignore the capability of aquatic organisms to accumulate higher concentrations of pollutants. References: 5 Russian.  
[245-6508]

## MICROBIOLOGICAL CONDITIONS AND WATER QUALITY IN LOWER DNEPR

Kiev GIDROBIOLOGICHESKIY ZHURNAL in Russian Vol 18, No 2, Mar-Apr 82  
(manuscript received 6 Feb 80) pp 51-57

ROSSOVA, E. Ya., MOROZ, T. G., KOKOREVA, R. A., SHAKHMAN, G. N. and  
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[Abstract] Microbiological studies of the Dnepr's waters have provided a description of the bacterioplankton in the river near Kherson. The dynamics of seasonal changes in the population of total bacterioplankton and heterotrophic bacteria are illustrated and discussed. Based on observations in 1978, it is found that processes of decomposition of organic matter and self-purification of water are most active in the branches of the Dnepr, the Koshevaya and Verevchikha Rivers in summer and in spring. Above and below Kherson the Dnepr is less polluted than within the city. Figures 5; references: 12 Russian.  
[245-6508]

UDC: 58.01/02:582.542.1

## RESISTANCE OF HILL REACTION TO VARIOUS DAMAGING AGENTS IN TWO SORTS OF WHEAT TRITICUM AESTIVUM (POACEAE)

Leningrad BOTANICHESKIY ZHURNAL in Russian Vol 67, No 4, Apr 82  
(manuscript received 2 Mar 81) pp 433-438

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[Abstract] A study was made to determine the level of organization of cell structures at which differences could be found in the thermal stability of varieties of plants. The study was performed on isolated chloroplasts, the intermediate stage of complexity between protein extracted from the cell and the intact cell. Thermal stability of one of the particular reactions of photosynthesis (the Hill reaction) was studied in the isolated chloroplasts. The rate of the Hill reaction was also compared in two sorts upon exposure to trypsin and detergents to determine whether there is a parallel in the sensitivity of the chloroplasts to the influence of damaging agents differing in their mechanism of action. The more heat-tolerant variety of wheat was also found to be more tolerant to exposure to the other damaging agents. The reason probably lies in a difference in the conformational mobility of chloroplast membranes, frequently related to resistance to damaging agents with various mechanisms of action. Figures 4; references 25: 8 Russian, 17 Western.  
[224-6508]

MEDICINE

UDC 614.2:001.83(100)(47+57)

DEVELOPMENT OF COOPERATION BETWEEN USSR AND LIBERATED NATIONS IN FIELD OF HEALTH IN LIGHT OF RESOLUTIONS OF 26TH CPSU CONGRESS

Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 1, Jan 82  
(manuscript received 10 Jul 81) pp 53-57

[Article by A. S. Gritsenko, A. A. Rozov, G. S. Orlov and Ye. P. Zhilyayeva, All-Union "Soyuzzdrazvzagrannostavka" Association, USSR Ministry of Health; All-Union Scientific Research Institute of Social Hygiene and Organization of Public Health imeni N. A. Semashko, USSR Ministry of Health]

[Text] In creatively developing a Peace Program as applied to the current international situation, the 26th CPSU Congress has advanced a new set of propositions, formulated in the report of the CPSU Central Committee to the party congress. The report further confirmed and developed the disinterested policy of strengthening international economic and scientific-technical cooperation and promoting the preservation of peace, detente and mutual understanding among peoples.

As Comrade L. I. Brezhnev noted in the report to the 26th CPSU Congress, "an important result of the party's international activity during the current period is the marked expansion of cooperation with countries liberated from colonial oppression"<sup>1</sup>.

In its relations with the developing nations the USSR follows a policy for the development of equal, mutually beneficial economic and scientific-technical cooperation, noninterference in internal affairs and full respect of sovereignty. This cooperation helps to consolidate political relations based on mutual understanding and friendship and rapprochement on the most important international problems. It assists liberated nations conducting independent international policies to realize progressive socioeconomic transformations in the interests of broad sections of the populations and to resist the neo-colonial pressures of the imperialist powers.

International cooperation in the field of health and medical sciences is part of the overall effort for strengthening and expanding economic scientific-technical and cultural relations between the USSR and developing nations.

Liberated nations are characterized by substantial transformations in various areas of socioeconomic life. These transformations include the health services, and certain countries after gaining their independence have been forced virtually to create these services starting from the central organs and ending with the simplest points of primary health-care assistance in the village district.

The Soviet Union cooperates with liberated nations to develop national health systems, to strengthen their material and technical base, to improve the medical service to the population, to train a national medical personnel, to control the most wide-spread infectious and parasitic diseases and so on.

Cooperation of the USSR with developing nations has a long history. As early as the 1920s and 1930s individual Soviet doctors worked in Asian countries rendering assistance to the local population. In the 1940s a 100-bed general hospital in Ethiopia and a large hospital with a polyclinic in Iran were constructed with the direct disinterested assistance of the Soviet Union.

But cooperation between the USSR and Asian and African nations in the field of health was particularly extended in recent decades. The Soviet Union presently realizes various forms of cooperation with the liberated nations.

Our country renders assistance in the development and strengthening of the material and technical base of national health care in developing nations by planning and constructing health institutions on the basis of mutually beneficial agreements. Thirty health institutions have been constructed in developing nations on the basis of such agreements, including a 400-bed hospital in Afghanistan, a medical faculty at the Polytechnical Institute in Guinea, a 200-bed hospital in Kenya and so on. In 1980 alone the Soviet Union cooperated in the planning, construction and equipping of 22 health establishments in seven Asian and African nations. Almost immediately after the rebirth of Democratic Kampuchea work was begun on reconstructing the general 500-bed Khmer-Soviet Friendship Hospital, opened in 1960 and forced out of the country as a result of the excesses of the Pol Pot clique; its first phase should be brought into operation at the end of 1981. Hospitals are presently under construction in Laos, the People's Democratic Republic of Yemen, the Congo and other countries with the participation of Soviet specialists. It should be noted here that the medical institutions created by the USSR in developing nations were planned with consideration of local conditions at the level of modern needs, were provided with the latest technological equipment and are models of progressive planning and organization. The stated form of cooperation is most effective when combined with the dispatch of Soviet medical specialists for work in these institutions.

Soviet equipment, medical instrumentation and medicines are sent to a number of developing nations. These deliveries are in some cases large in volume and include all equipment necessary for work in medical institutions. Moreover, they are made exactly when and, so far as possible, in the form and volume required by the receiving country. Such was the case, for example, in the Algerian city El Asnam, which after suffering an earthquake received in the shortest time possible two Soviet health brigades totaling 30 people. The brigades contained surgeons, therapists, specialists in infectious diseases, anesthesiologists, surgical and general nurses, laboratory nurses, etc. The Soviet specialists brought virtually all necessary medical equipment, surgical instrumentation, medicines and dressings, linen, tents and ambulances in order to immediately begin rendering medical assistance to the population.

Deliveries of Soviet vaccines and sera are important for health in developing nations. Let us recall that the Soviet smallpox vaccine made an important contribution to the liquidation of smallpox in the world. In accordance with the policy of the WHO and on a bilateral basis for this program, the Soviet Union transferred gratis more than 1.5 million doses of the vaccine. The Soviet smallpox vaccine was used for smallpox liquidation measures in many developing nations, for example in Afghanistan, Bangladesh, Burma, Zambia, India and others. Soviet doctors participated directly in smallpox liquidation programs in a number of developing nations.

In support of the expanded immunization program conducted by WHO the Soviet Union supplies vaccines for immunization to developing nations. More than 12 million doses of various Soviet vaccines and sera were transferred to the WHO as a voluntary contribution of the USSR. A large portion of these vaccines have been used for the populations of Nicaragua, Angola and Mozambique.

An important form of cooperation with developing nations is the dispatch of Soviet specialists for work in these nations in accordance with the appropriate agreements. "Tens of thousands of Soviet specialists selflessly labor at construction sites in the countries of Asia and Africa, in industry and agriculture, in hospitals and educational institutions," said Comrade L. I. Brezhnev in his report to the 26th CPSU Congress<sup>2</sup>.

A large group of Soviet physicians is presently working in more than 25 countries of Asia and Africa. Especially large groups of Soviet medical specialists work today in Algeria, Afghanistan, Tunisia, Angola, Guinea, Mozambique and Ethiopia. It should be noted that the number of Soviet physicians presently working in liberated nations is nearly 50% greater compared with the start of the 9th Five-Year Plan.

The Soviet Union sends an experienced and qualified personnel to the developing nations. Of the total number of Soviet physicians presently working abroad about 500 possess the university degrees of Candidates and Doctors of



Medical Sciences, It is important to note that in many cases Soviet physicians work in developing nations in the capacity of leading specialists and consultants.

The large quantity of work performed by Soviet doctors, their high professional qualifications and moral qualities have endeared them to the populations and health service managers in liberated nations. The personal contacts of Soviet specialists with the local population have helped to dispel those false notions about the Soviet Union that were for many years inculcated and are being inculcated in the populations of developing nations by bourgeois propaganda.

Soviet physicians conduct significant scientific research activity, systematize and analyze accumulated experience and participate in scientific conferences, which they often initiate. Scientific cooperation on the development of questions of mutual interest is underway with a number of the developing nations that have accumulated a significant scientific potential. Such cooperation has been arranged with the Republic of India, the Syrian Arab Republic, the People's Revolutionary Republic of Guinea and others. Thus, for a number of years Soviet and Guinean scientists have conducted joint investigations in Guinea at the Scientific Research Microbiological Virological Laboratory to develop effective measures for the prevention and control of a number of infectious diseases.

In the report to the 26th CPSU Congress L. I. Brezhnev noted that "our nation, insofar as it is able, assists many liberated nations to train cadres--engineers, technicians, skilled workers, doctors and teachers"<sup>3</sup>.

In attempting to expand or organize the training of doctors in their nations, the governments of developing nations have invited Soviet instructors to work at university medical faculties and in medical institutes. Soviet medical instructors are currently working in Laos, Guinea, Algeria, Zambia, Ethiopia, Afghanistan and the Mali Republic. This form of cooperation is made especially promising by the fact that Soviet specialists not only acquaint their students with the appropriate scientific disciplines and the latest achievements of medical sciences and health but also strive to assure training adequate to the health requirements in these countries.

The training of students from developing countries in the universities and medical institutions of the Soviet Union is conducted in accordance with bilateral agreements and stipends of WHO. Representatives from the developing nations presently comprise a majority among the several thousand students, postgraduates and nondegree medical students from nearly 100 nations that are undergoing training on the basis of Soviet medical educational and practical institutions.

While the Soviet Union renders developing nations disinterested assistance for training national health cadres, the politics of the Western capitalist governments has led to a considerable loss of qualified personnel from the developing nations. According to the data of an investigation conducted by UNCTAD, in 1961-1972 the developing nations gave the USA, Canada and England 23,000 specialists, of which 20% were physicians<sup>4</sup>. The monetary gain to the West from the immigration of this qualified work force reached approximately 50 million American dollars and exceeded the combined quantity of assistance from the USA, Canada and England to developing nations during the same period, which comprised 46 million USA dollars<sup>5</sup>.

Subsequent data, also gathered by UNCTAD, indicate the persistence of such phenomena. Thus, materials prepared for UNCTAD by the Marga Institute (Sri Lanka) show that the total income of England in 1968-1974 from the emigration of doctors out of Sri Lanka to England comprised 56 million American dollars, while the "donor country" sustained a corresponding material loss<sup>6</sup>. During the same period assistance to Sri Lanka from England for development purposes comprised about 57 million American dollars<sup>7</sup>.

The "drain" of specialists, including medical, from the developing countries is promoted by the methods of neocolonial "assistance", aimed at preserving in liberated nations systems for cadre training by the Western model, on the basis of Western programs and teaching materials with the consolidation of European languages as the required languages of instruction. This comprises a specific manifestation of the fundamental distinction of "assistance", in the colonialist model, provided by the countries of the West to developing nations. It is no accident that it was the USSR with the active support of the developing nations that prompted the WHO to adopt the World Health Assembly (WHA) Resolution 22.51 concerning the "brain drain" and subsequently to undertake a broad study of this problem.

The example and experience of the Soviet Union is of vast significance for the developing nations. International conferences, seminars and symposia, including those in accordance with the WHO program, are regularly held in the USSR and involve representatives of the medical community of developing nations. A recent striking indication of the appeal and value of the Soviet health experience for the developing nations was the successful WHO/UNICEF conference held in Alma Ata in 1978 on primary medical assistance. Delegations from more than 130 governments participated. In the course of the discussion the delegates from a number of developing nations (Uganda, Ethiopia, Equatorial Guinea and others) spoke of the politics of neocolonialism and the "brain drain", the luring of specialists from developing nations. The majority of delegates of developing nations, in particular Algeria, India, Indonesia, Mozambique, Peru and others, supported the thesis, advanced by the USSR and other socialist nations and borne out by their practical experience, that primary health care can be developed effectively only as an inseparable part of a national health

system. This position was consolidated in the Declaration and Recommendations of the Alma Ata Conference, where international recognition was accorded anew to the principles of government responsibility for the health of the population, the combining of therapeutic medicine with prophylactic, health care accessibility, etc., which have been realized in the practice of socialist health care and were recommended to the nations in WHA Resolution 23.61.

The representatives of the developing nations participating in the conference were greatly impressed by their on-site acquaintance with the work of Soviet health institutions, which included all components of the medical service system in the cities and villages. Familiarity with the practical experience of Soviet health care is now assisting the developing nations to realize the recommendations of the Alma Ata Conference.

The long-term experience of cooperation between the USSR and the developing nations confirms its effectiveness and the progressive nature of these principles on which it is constructed. All this justifies its further development and improvement.

In the report at the 26th CPSU Congress L. I. Brezhnev said "no one can doubt, comrades, that the CPSU will continue to follow a policy for the development of cooperation between the USSR and the liberated nations, for the strengthening of the union between world socialism and the national liberation movement"<sup>8</sup>.

The USSR and the developing nations adhere to the same position with respect to the affirmation of the principles of equality, sovereignty, mutual advantage and responsibility in cooperation. A guarantee of the broad prospects for fruitful cooperation is the fact that the USSR from its very first steps in the international arena has not only proclaimed but has directly realized the foregoing principles in the practice of its international relations, including those in the field of health.

The broad scientific-technical cooperation of the Soviet Union with the developing nations is based on a community of interests. The USSR recognizes that a radical solution to the most acute problems in the developing nations, including those in the field of health, is impossible in detachment from the general questions of the lessening of international tension and the attainment of real disarmament. Unfortunately, certain developing nations contain militaristically inclined elements and use no small portion of their financial resources for armaments, resources that could have been used for the purpose of creating and, in particular, protecting and strengthening the health of the population. This in considerable measure reduces the rate of return from national efforts and from international cooperation in the field of health.

In supporting the developing nations in the solution of urgent problems in their economy, culture and health, the Soviet Union deepens its policy for radical improvement of the international situations, the consolidation of peace and control over the arms race. The peace-loving politics and peace initiatives advanced by the USSR find increasingly broad support among progressive circles in developing nations.

#### FOOTNOTES

1. L. I. Brezhnev, "Otchetnyy doklad Tsentral'nogo komiteta KPSS XXVI s 'yezdu KPSS i ocherednyye zadachi partii v oblasti vnutrenney i vneshney politiki" [Report of CPSU Central Committee to 26th CPSU Congress and Immediate Tasks of the Party in Domestic and International Politics], Moscow, Politizdat, 1981, p 15.
2. Ibid., p 16.
3. Ibid.
4. UNCTAD Document TD/B/C.6/28; TD/B/AC.4/10, 20 March 1978, p 11.
5. Ibid.
6. Ibid., TD/B/C.6/AC.4/4, 19 December 1977, p 9.
7. Ibid.
8. L. I. Brezhnev, "Otchetnyy doklad Tsentral'nogo komiteta KPSS XXVI s 'yezdu KPSS i ocherednyye zadachi partii v oblasti vnutrenney i vneshney politiki" [Report of CPSU Central Committee to 26th CPSU Congress and Immediate Tasks of the Party in Domestic and International Politics], Moscow, Politizdat, 1981, p 20.

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UDC 616-073.75+616-073.916+615.849.1]:061.62:[608.1/.4+347.77.018

INVENTIVE AND PATENT-LICENSING WORK OF MOSCOW SCIENTIFIC RESEARCH  
ROENTGENORADIOLOGICAL INSTITUTE

Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 27, No 2, Feb 82  
(manuscript received 24 Jul 81) pp 58-61

[Article by N. K. Sviridov, V. N. Varfolomeyeva, T. I. Sokolova, L. V. Arapova  
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[Text] The work of inventors and innovators in various scientific and technological fields is of great significance for the acceleration of scientific and technical progress.

Inventive and patent-licensing work at the Moscow Scientific Research Roentgenoradiological Institute (MNIRRI) is directed by the institute's Patent-Informational Department (PIO). The department was organized in 1972. During the 9th Five-Year Plan all institute-staff research activity was directed by a single patent engineer. A patent group consisting of four staff personnel was established recently, and the work of the remaining department personnel (a total of 13 people in the department) has definitely helped to extend the inventive work of the institute's staff. The institute employs 580 people, including 260 scientific and engineering workers. The structure of the institute includes 10 scientific subdivisions. The main subdivisions are the physicotechnical, radiological, X-ray diagnosis, radioisotope diagnosis and high-energy sections.

The institute's invention work is regulated by USSR Ministry of Health Orders No. 990 of 13 December 1973 and No. 700 of 3 July 1979. The main goal of this work in the 10th Five-Year Plan was to activate the creative power of inventors and innovators directed to generation of new, more efficient methods of radiation diagnosis and therapy, improvement of existing methods of X-ray and radioisotope examinations and of radiation and combined methods of patient therapy and directed to resolution of medicotechnical tasks for new and existing roentgenoradiological equipment.

The inventive, innovative and patent-licensing work is planned in annual PIO work plans. Furthermore, invention planning is included in the formulation of MNIRRI scientific research work (NIR) plans for the five-year plan and for each year. The PIO personnel jointly with the research-theme developers conduct a patent-informational study of proposed investigations prior to the inclusion of the NIR in the institute plan (N. K. Sviridov et al.), as a result of which patentable NIR is identified. The table presents the quantity of planned and patentable NIR from 1976 to 1981.

A trend toward a decline in the quantity of NIR at the institute can be clearly seen in the table. This is due to the fact that the RSFSR Ministry of Health has recommended comprehensive investigations.

With respect to patentable NIR an invention-work plan is being composed in the PIO for each year and includes the names of patentable topics, the names and quantity of prospective claims for inventions on each of the themes, the surnames of the creators of prospective technical solutions. Undoubtedly, the plan incorporates only those technical solutions whose "contours" are clearly defined. Interest in inventive work has grown markedly at the institute, as was shown by the overfilling of the invention-work plan in 1979-1980. The plan will apparently be greatly overfilled in 1981, since 17 invention claims were planned for the year, while during the first half of the year 21 claims were forwarded to the All-Union Scientific Research Institute of Government Patent Examination (VNIIGPE). Thus, in 1981 one claim was proposed for X-ray tube development. During the first half of the year two claims were submitted to the VNIIGPE for X-ray tubes. No claim was offered for development of the currently more promising X-ray diagnostic system--the X-ray computer tomograph. Eight claims were submitted for "X-ray apparatus", while three claims were planned, and so on. Most invention claims were made by staff personnel of the physicotchnical section. Four claims were planned for the medical subdivisions for 1981.

Providing the institute personnel with information is very important for increasing the level of inventive and patent-licensing work. A reference collection including both patent as well as scientific-medical and scientific-technical documents has been established in the PIO. In order to select patent documents for each of the lines of research in the "Scientific Bases of Clinical Roentgenology and Radiology" problem under development at the institute, a thematic list was composed including articles and entries of the International Classification of Inventions and National Classifications of Inventions. PIO staffers have published articles on this question (V. N. Varfolomeyeva; N. K. Sviridov and V. N. Varfolomeyeva; N. K. Sviridov et al.). Bibliographic and annotated lists on computer tomography, X-ray diagnostic tubes, fluorography, mammography, X-ray contrast substances, etc., have been prepared to assist investigators. A bibliographic guide "Instruments and Systems for Regulating Parameters in X-ray Diagnostic Apparatus"

and two radiation therapy guides are in the preparation stage. The guides circulate in the institute sections, are sent to chief roentgenologists and radiologists and to roentgenology and radiology faculties at RSFSR medical institutes.

The formulation of invention claims involves the inventors together with the patent-group staff. The responsibilities of the patent group include consultations with inventors on all questions of claim composition, indirect participation in the patent-informational search relating to the originality of the claimed object by means of the composition of search regulations, formulation and forwarding of the documents to the VNIIGPE and monitoring correspondence with respect to the claim. The description of the invention is composed primarily by the actual inventor.

Upon receipt of an author's certificate an order is drawn up at the PIO for an incentive fee to the invention authors. If the invention was introduced at the institute a fee for the introduction of the invention is computed and an order for its payment drawn up.

From 1969 to the first half of 1981 institute personnel made 208 claims for inventions to the Government Committee on Inventions and Discoveries: 85 from 1969 to 1975, 12 in 1976, 11 in 1977, 13 in 1978, 31 in 1979, 35 in 1980 and 21 claims in the first half of 1981. It is apparent that the number of claims increased abruptly in 1979. Of the 208 claims, 125 were recognized as inventions, comprising 60% of the claims made. The majority of invention claims were submitted by institute personnel. Inventions have also been made in the plan of execution of comprehensive themes with personnel of other organizations, such as the Mosrentgen Plant, the Leningrad "Svetlana" Association, the All-Union Scientific Research and Testing Institute of Medical Technology, the All-Union Scientific Research Institute of Radiation Technology, etc. With respect to the number of author certificates obtained during the 10th Five-Year Plan among scientific research institutes of the medical type, the Institute of Medical Radiology, USSR Academy of Medical Sciences, occupies first place (83 author certificates), second place is held by MNIRRI (72 author certificates) and third by the All-Union Oncological Scientific Center, USSR Academy of Medical Sciences (49 author certificates).

The institute has patented an invention in Hungary from author certificate No. 563750, the "Scanner" ("apparatus for determining the distribution of a radioactive preparation in the body"). A license was sold for this invention in Hungary in 1980. The license agreement came into force in December 1980. Patent-group workers along with the workers of the radioisotope diagnostics sections, the authors of the "Scanner" invention, have been involved in preparing this invention for patenting and licensing since 1976. This was the first experience for the MNIRRI in the foreign patent and license-sale of an invention. Furthermore, this was the first license sold abroad in the system of institutions of the RSFSR Ministry of Health.

The MNIRRI has conducted many years of joint work with the "Gamma" company (Hungary) in the development and creation of modern nuclear diagnostic instruments. The "Gamma" company is the major supplier to the USSR of high-quality instruments for radionuclide diagnostics. The MNIRRI has developed methods for the medicotechnical testing of instruments, new instruments for nuclear medicine and has improved currently available instruments. The "Scanner" apparatus in author certificate No. 563750 is an improved version of the MNIRRI-Gamma MB-7500 scanner released by the Gamma company (Hungary). The new instrument is used to evaluate the distribution of nuclide preparations both in individual organs and in the whole body and affords the possibility of obtaining a profile simultaneously from two selected regions of the patient's body. Technical documentation was developed for the "Scanner" instrument, and an experimental model of the instrument has been created in the institute's experimental shop.

A series of inventions are currently being patented jointly with the Scientific Research Institute of Medical Radiology, USSR Academy of Medical Sciences, in the Federal Republic of Germany, France and Canada.

The institute's employees have developed numerous innovative suggestions. From 1972 to the first half of 1981, 204 innovations of local significance and 17 innovations of branch significance were recognized.

In his Report to the 26th CPSU Congress, General Secretary of the CPSU Central Committee L. I. Brezhnev noted that a most important sector today is that of the introduction of scientific discoveries and inventions. The activity of scientific research institutes and the nation's other institutions in the area of invention and innovation "... must be evaluated not only by the number of claims made nor even by the quantity of author certificates obtained, but primarily by the number of introduced inventions, by their significance for the national economy and by the competitiveness in foreign markets of products created on the basis of these inventions" ("Voprosy izobretatel'stva" [Questions of Invention]).

The introduction of inventions at the institute is conducted in agreement with USSR Ministry of Health Order No. 939 of 31 December 1968 and the RSFSR Ministry of Health Letter of 31 March 1980.

In accordance with the plan of introduction of inventions for the 11th Five-Year Plan, 12 inventions are planned for introduction at the institute in 1981. Furthermore, three developments protected by author certificates should reach industrial production in 1981. They are the assembly-line production of "Stabilirent-SI-10-RN" (author certificate No. 756686) at Mosrentgen Factory, "Rentgenokimografa" (author certificate No. 716554) and "Instrument for calibration and verification of circulographic apparatus". The latter was released in a quantity of eight assemblies by the institute's experimental shop and introduced at the Ufa Republic Clinical Hospital, the Omsk Oblast Clinical Hospital, the Kazakh Scientific Research Institute of Roentgenology and Radiology (Alma Ata) and at other institutions.



In accordance with the PIO work plan for 1981, the RSFSR Ministry of Health must be presented with documentation for seven inventions introduced at the institute in order to resolve the question of use of these inventions at institutions of the RSFSR Ministry of Health.

The MNIRRI PIO should be capable of rendering great assistance in inventive and innovative work to chief roentgenologists and radiologists and RSFSR roentgenology and radiology chairs. A patent library is being established in the PIO, which may be used by chair personnel. Copies of invention descriptions for patents and author's certificates can also be prepared in accordance with chair requests. In 1979-1981 the MNIRRI appealed to 36 RSFSR roentgenology and radiology chairs asking that they send plans for inventive and innovative work to the MNIRRI. Responses to the request were obtained from only five chairs.

For successes in inventive and innovative work the MNIRRI was awarded honorary certificates of the Moscow City Society of Inventors and Innovators in 1978, 1979 and 1980, and, in 1981--for attaining high achievements in inventive and innovative work and for participating in the USSR Exhibition of Achievements of the National Economy--it was awarded an Honorary Diploma of the Coordinating Center of CEMA member nations for medical-technology development. In 1980 the MNIRRI took first place for inventive work in a socialist competition in Moscow among scientific research institutes and planning-construction organizations of the medical type.

The experience from the work of the PIO indicates the need for creating special patent-invention groups in scientific-medical information sections, whose cooperative work will assure the success of inventive and innovative work in scientific research institutes of the medical type.

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UDC 576.893.161.13.097.21

CHANGES IN VIRULENT PROPERTIES OF PATHOGEN STRAINS OF ZOONOTIC SKIN  
LEISHMANIA IN PASSAGE THROUGH PHLEBOTOMUS PAPATASI

Moscow MEDITSINSKAYA PARAZITOLOGIYA I PARAZITARNYYE BOLEZNI in Russian  
Vol 50, No 6, Nov-Dec 81 (manuscript received 5 Apr 81) pp 19-22

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[Abstract] To study *Phlebotomus papatasi*, practically the only carrier of  
*Leishmania major* to man, *Ph. papatasi* mosquitoes were force-fed various  
virulences of *L. major* to replicate natural distribution and virulence of the  
disease. Ratios of clone low- and high-virulence pathogens, ranging from  
1 : 1 to 50 : 1, were also administered. After 3-6 days the intestinal content  
of surviving mosquitoes was planted on a culture, and the virulence of the  
product was measured by infecting golden hamsters and white mice. The natural  
and clone pathogens passed through the *Ph. papatasi* showed that the development  
of both low- and high-virulence strains of *Leishmania* occur without changes  
during their sojourn within the mosquitoes. In mixed pathogens, the highly  
virulent strains tended to become predominant, especially where the length  
of time amounted to 5-6 days after infection. References: 13 Russian.  
[139-12131]

IMPORTED OVALE MALARIA IN RSFSR

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Vol 50, No 6, Nov-Dec 81 (manuscript received 6 May 81) pp 27-32

NEMIROVSKAYA, A. I., MOROZOVA, N. K., NEKIPELOV, V. Ya. and YASINSKIY, A. A.,  
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[Abstract] Data for 1973-1980 concerning the incidence of ovale malaria show 204 cases, with 134 appearing in Soviet citizens returning from various African countries and 70 among Africans from 23 countries who were sojourning in the republic. Although cases were reported that originated in all parts of Africa, the greatest frequency occurred in Soviet citizens returning from Guinea (46), Equatorial Guinea, the Central African Republic and the Congo. Immunity to various types of malaria among natives explains the sharp difference in Plasmodium ovale incidence between Soviet citizens and Africans. The authors suspect that Soviet citizens also contract other types of malaria which are effectively treated by delagyl or other aminoquinolines. Native immunity to P. vivax is related to the absence of antigens of the Daffy group on the erythrocytes of negroids. Africans from non-immune native groups are apparently carriers of P. vivax, but more information is needed. References 35: 24 Russian, 11 Western.  
[139-12131]

DYSENTERY AMOEBA INFECTION OF POPULATION IN SOUTHERN PARTS OF RSFSR,  
REPORT I: PROTOZOOLOGICAL STUDY DATA

Moscow MEDITSINSKAYA PARAZITOLOGIYA I PARAZITARNYYE BOLEZNI in Russian  
Vol 50, No 6, Nov-Dec 81 (manuscript received 20 May 81) pp 41-44

PRODEUS, T. V., Institute of Medical Parasitology and Tropical Medicine imeni  
Ye. I. Martsinovskiy, USSR Health Ministry, Moscow

[Abstract] Expeditions studied the coastal lowland locations of Derbent, and the settlements Syrtych and Kuvlig in the Tabasaranskiy Rayon in the Dagestan ASSR, to determine the incidence of amoebic dysentery. Derbent and Syrtych are on the coastal plain; Kuvlig is in the piedmont. A formalin-ether precipitation method was used to study fecal material gathered in the settlements. Results showed the presence of 8 different protozoa, including 5 amoebas and 3 flagellates. Dysentery amoeba accounted for 3.8-9.6% of all protozoa in Derbent, and for 9.7-12.9% in Syrtych. The relatively high

incidence of protozoa illnesses in Syrtych was constant throughout the year, while in the less affected settlement of Kuvlig, all infections except those from *Lamblia intestinalis* decreased in the spring of 1978. In both test years of 1977 and 1978 and in both settlements, the 15-40 age group was most affected. Conditions in the coastal lowland were found to be more favorable for the transmission of *Entamoeba histolytica* infections. Figure 1, references 17: 14 Russian, 3 English.  
[139-12131]

UDC 340.624.1:614.821:629.73

#### FORENSIC MEDICAL CLASSIFICATION OF AVIATION INJURIES

Moscow SUDEBNO-MEDITSINSKAYA EKSPERTIZA in Russian Vol 25, No 1, Jan-Mar 82 (manuscript received 25 Jun 81) pp 18-20

POPOV, V. L., Chair of Forensic Medicine, Military Medical Academy imeni S. M. Kirov, Leningrad

[Abstract] A classification scheme was devised for the trauma encountered in aviation accidents, based on the recognition that injuries can occur in several different types of situations: a) in-flight injuries, b) wounds and injuries resulting from impact of the aircraft on crashing, and c) trauma sustained on ground (in and out of the aircraft). Irrespective of the setting, the factors responsible for actual trauma can be classified as mechanical, thermal, chemical, and/or barometric. A chart is provided of the forensic medical classification scheme. Figures 1; references: 4 Russian.  
[259-12172]

UDC 340.661:614.86:629.73

#### ADVISABILITY OF COMPARISON OF FORENSIC MEDICAL EXPERT DATA ON FLIGHT CREWS WITH DATA FROM ONBOARD RECORDING DEVICES

Moscow SUDEBNO-MEDITSINSKAYA EKSPERTIZA in Russian Vol 25, No 1, Jan-Mar 82 (manuscript received 5 Jan 81) pp 21-22

ALPATOV, I. M., Moscow

[Abstract] Observations are presented on the manner in which medical findings concerning injury of flight crews and data obtained from onboard recording instruments mutually complement each other in arriving at explanations of the trauma sustained by the flight personnel and their putative behavior patterns during an accident. As yet, however, the information provided by the recording

devices has not received the acceptance that it should have in aviation medicine. Figures 2 (one consists of 3 photos--flight data record, equipment involved and injury sustained).

[259-12172]

UDC 340.661:617-001-036.88]-07(470.23)

ANALYSIS OF FATAL CAR ACCIDENTS IN LENINGRAD OBLAST AND WAYS TO IMPROVE MEDICAL ASSISTANCE

Moscow SUDEBNO-MEDITSINSKAYA EKSPERTIZA in Russian Vol 25, No 1, Jan-Mar 82 (manuscript received 27 Jan 81) pp 27-29

BALLYUZEK, F. V., ZASLAVSKIY, G. I. and MATYSHEV, A. A., Bureau of Forensic Medical Expertise, Leningrad Oblast; Chair of Hospital Surgery, Leningrad Sanitary Hygiene Medical Institute, Chair of Forensic Medicine, Military Medical Academy imeni S. M. Kirov, Leningrad

[Abstract] A survey of the 1977-1978 period has shown that traffic accidents accounted for 25% of all the accidental deaths in the Leningrad Oblast, and that traffic deaths are increasing at an annual rate of at least 10%. In addition, it has been established that ca. 70% of the pedestrians and 50% of the drivers who meet death in this manner are inebriated; furthermore, almost 85% of the motor cyclists who are killed in accidents involving cars have excessive levels of alcohol in the blood. Evaluation of the medical assistance rendered to the victims of such accidents has shown that it is generally unsatisfactory. As a rule no medical assistance is given prior to the arrival of an ambulance, and the ambulance teams seldom do more than transport the patients to a hospital (at times to a wrong hospital and several trips may have to be made before an emergency facility is reached). The emergency medical personnel are slow to commence treatment and take recourse to time-consuming consultations with specialists, so that two to five hours may elapse between the time when the patient is first seen and treatment instituted. Emergency surgery is generally limited to the head, while the abdominal, chest, and pelvic areas are ignored; 38% of the cases that need surgery never receive it. In short, the medical emergency personnel appear to be poorly trained and require further intense advanced education in emergency medicine, measures which are currently being taken. References: 8 Russian.

[259-12172]

HEALTH RESORT RESOURCES AND RESORT-SANATORIUM NETWORK IN WESTERN SIBERIA

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY  
in Russian No 2, Mar-Apr 81 pp 5-9

[Article by N. M. Starikov, Tomsk Scientific Research Institute of  
Balneology]

[Text] In addition to development of industry in Western Siberia, the Communist Party and Soviet government devote enormous attention to meeting the social and cultural demands of residents of Siberia, including medical and sanatorium-resort care.

Sanatorium-resort care and organized recreation play a large part in improving the indicators of public health, increasing labor productivity and, ultimately, strengthening manpower resources. The need for sanatorium and resort treatment and rest increases annually. It is justifiably indicated that resort therapy and rest must be organized in the customary climate, without distant travel, change in time zone or disruption of the body's biological rhythm. This applies, first of all, to patients with diseases of inflammatory etiology, cardiovascular, bronchopulmonary systems, since they most often react adversely, sometimes for a long time, to acclimatization and adaptation processes. As far back as 1917, N. V. Vershinin, who fought for development of health resorts in Siberia, wrote: "... Siberia, more than any other region, needs local resort therapy. Because of its rigorous climate, it produces a large number of patients who need climatotherapy and balneotherapy. Far from all such patients are able to travel thousands of versts [old Russian unit of length, 1 verst = 1.0668 km] to resorts in European Russia or abroad, but ... this also has an adverse effect on the results of treatment itself: having become accustomed to a milder climate, when a resident of Siberia returns to his familiar environment ... he becomes more sensitive to the deleterious effects of the rigorous climate of Siberia."\*

In spite of the fact that there were some descriptions of the natural therapeutic factors of Western Siberia even in prerevolutionary times and after the Great October Socialist Revolution, the most comprehensive and planned studies thereof only began in the late 1950's.

\*Vershinin, N. V., in "Tomskiy gubernskiy 1-y s"yezd vrachey. Trudy" [First Congress of Physicians of Tomsk Province. Proceedings], Tomsk, Vyp 2, 1917, pp 108-117.

Intensification of exploratory oil and gas drilling, comprehensive development of raw material [mineral] deposits have broadened significantly the boundaries of hydrogeological structure of Western Siberia, making it possible to discover and determine the distribution of mineral waters with different chemical and gas composition, as well as to study in greater detail the sources of silt and sapropel [organic mud] deposits, peat and salt lakes. Resort and therapeutic localities have appeared on the map of Western Siberia, while resorts, sanatoriums, rest homes and other modern recreational institutions have appeared in oblasts and krais.

Thus, before the revolution, there was not a single resort, sanatorium or single therapeutic locality in Tyumenskaya Oblast. At present, in addition to oil and gas, therapeutic mineral springs and deposits of sapropel therapeutic mud have been discovered in the northern part of this oblast. There are balneotherapeutic facilities, with sodium chloride and iodobromine mineral springs in the Oblast Clinical Hospital, Polyclinic No 1 for Tyumen' miners, as well as the Ishimskiy, Yarskiy, Zavodoukovsk, Khanty-Mansiysk, Tobol'sk and Abatskiy treatment facilities. Since 1947, there has been a 100-bed mud-therapy facility in operation on Lake Akhmanka in Nizhne-Tavricheskiy Rayon. The 200-bed balneological resort, Bol'shoy Taraskul', near Tyumen', began to accept patients in 1977, and since that time it has been expanding, so that today it has a 1360-bed capacity. There are a pediatric climatotherapy and balneological sanatorium, "Taraskul'", three rest homes, sanatoriums-preventoriums and rest centers of industrial enterprises. In that oblast, there is an unlimited reserve of peat and sapropel suitable for therapeutic use at the resorts or elsewhere. The existence of climate-resort localities with thermal mineral springs opens the way for developing local health facilities in Yalutorovsk, Kondinskiy, Surgutskiy, Yarkovskiy and other areas, including institutions that use the therapeutic mud from the Lebyazh'ye, Tolubayevo, Sey-Teul', Maloye Arakchino and Malye Taraskul' water reservoirs [rivers?].

On the territory of former Narymskiy Kray in Tomskaya Oblast, development is in progress of springs of mildly sulfide sodium chloride water in Chazhemto, thermal iodobromine mineral water in the new mining city, Strezhevoy, and there are plans to make therapeutic use of other mineral springs and to outfit peat therapy facilities in a number of regions.

Enormous deposits of floodplain peat and sapropel mud with high levels of biologically active constituents have been studied near the major cities of Tomsk, Kolpashev and Strezhevoy. There are a children's sanatorium, 3 rest homes, 8 sanatorium-preventoriums and 20 rest centers of industrial enterprises in operation in Tomskaya Oblast. They are located on the Ob' and Tom' Rivers in picturesque suburban cedar, pine forests and beech groves.

Even before the revolution, an attempt was made, which turned out to be fruitless, to open a resort in the suburbs of Omsk (Chertova Yama). The natural therapeutic factors of salt lakes, which were known to the residents, were not used, although the scientific and medical community repeatedly discussed this matter. The interesting dissertation of the physician, N. S. Kastorskiy, "On the Chemical Composition of Mineral Springs of Baraba" (1911), did not interest anyone. At the present time, in addition to the forest and park zone in Omsk, there is a balneophysiotherapeutic oblast facility, with

40 tubs and a mud therapy facility. There is a boarding house. This facility's capacity is over 1000 patients per day. There, sodium chloride mineral water with a considerable concentration of iodine, bromine and silicic acid from wells is used for therapeutic baths, irrigation, showers and intake, as well as silt mud from Ul'dzhay Lake and other physical therapy resources. Local therapeutic factors are used extensively at the Kolos and Tavricheskoye sanatoriums, which opened in recent years.

In Omskaya Oblast, there are 3 rest homes, 2 children's sanatoriums, 18 sanatorium-preventoriums with 1500 beds and many summer recreation [rest] centers of enterprises. Patients with pathology of the skeletomuscular system, nervous system, respiratory organs, gynecological diseases, etc., are treated at the balneotherapeutic facility and sanatorium-preventoriums. There are some promising areas for the construction of resorts, sanatoriums, mud therapy facilities (Ebeyty, Ul'dzhay, Krivoye, Solenoye Lakes), mineral water for use at health resorts or at home, including mineral water for bottling purposes.

The Ozero Karachi resort has been known in Novosibirskaya Oblast since 1889. The therapeutic properties of mud and brine from this lake were already known in the 18th century. Patients stayed in dilapidated tents and mud huts, while the therapeutic wealth of the lake was exploited mercilessly by merchant lessees. Before the revolution the resort was on the verge of a disaster.

After nationalization, the resort revived. At the present time, this is a resort that has 880 beds. In 1958, a 125-bed republic-level children's sanatorium was opened there. A sanatorium for parents with children is under construction. In addition to mud application and salt water baths, chloride-hydrocarbonate sodium water recovered from a depth of about 1000 m is used in conjunction with other treatment for patients with gastrointestinal diseases. Karachi mineral water is being bottled. The Lake Karachi resort is being constantly upgraded and expanded. Instead of wood buildings with many-bed wards, there are now sleeping units several stories tall, with one- and two-bed rooms, halls and recreation rooms. There is a well-equipped mechanized mud bath facility with salt-water departments, medical diagnostic offices and laboratories, a club, dining room, aerosolarium, beach and boat dock. There is constant construction at the resort. It will be able to handle up to 1500-2000 patients at a time. Two comfortable sanatoriums have been deployed in a suburb of Novosibirsk: Rechkunovskiy with 750 beds and Zayel'tsovskiy Bor with 180 beds; a 200-bed interkolkhoz sanatorium was built in Krasnozerskiy Rayon. A department of rehabilitation therapy for patients who have sustained myocardial infarction was opened at the Rechkunovskiy sanatorium. There is radon water with up to 24 nCi/l radioactivity at Zayel'tsovskiy Bor. An interkolkhoz sanatorium is under construction in Kupinskiy Rayon, near the Novo Klyuchi Lake that has therapeutic mud. The natural therapeutic resources make it possible to utilize silt mud in seven rayons, including Chistozernyy and Kyshtovskiy, as well as 16 sapropel sources in 6 other regions, including the region of Lake Plyukhino near Novosibirsk. In Novosibirskaya Oblast, there is regional distribution of iodobromine and bromine, radioactive, carbonate, silicate and mineral water, which does not contain specific components or have specific properties. Comprehensive studies of these waters revealed that most of them can be used



at health resorts and elsewhere. There are more than 30 sanatorium-preventoria in this oblast, with almost 3000 beds, as well as 4 children's sanatoriums and 4 rest homes.

Of greatest recreational value in the mountainous part of Siberia is the Altay with its abundant animal and plant kingdoms, mountain rivers, lakes and glaciers. However, due attention is not being given to investigation of recreational and therapeutic resources of Altay, although the territory of Gornyy Altay alone is much larger than the territory of some large European countries. The climate of this region is characterized by many hours of sunshine (from 1792 to 2634 hours in the high-altitude valleys), rarefied air and very clear atmosphere. Solar radiation constitutes up to 142 kcal/m<sup>2</sup>. There, some therapeutic localities with unique climate and resort resources for Siberia are situated, including the regions of lakes Teletskiy, Mazherok, Chergi, Ayskiy, Barangoly, Chemal, Belokurikha and many others. There are tourist and recreation centers in part of these localities.

For example, the picturesque locality of Chemal has been a summer recreation site since 1907, as a mountain climate area. Since 1926, there has been a tuberculosis resort with 250 beds, where the mild curative properties of the climate are used, koumiss and antibacterial therapy is administered. The All-Union resort, Belokurikha, is situated in the foothills of the Altay. The nitrogen, mildly mineralized, radioactive, silicate alkaline hot springs have been famous since the 18th century. The local residents used them as far back as 1867. In spite of the persistent demands of scientists to make use of the curative properties of the radioactive spring and its popularity, the Belokurikha resort was in a run-down condition before the revolution. In 1925, there were only vacation homes for 50 people, which were open only in the summer. At the present time, on the territory of this resort there are 6 sanatoriums (Belokurikha, Katun', Altay, Tsentrosoyuz and 2 for children) and an outpatient sector, which together can handle almost 3000 people at a time. A new 500-bed sanatorium, Sibir', is being opened for parents with children; a 1000-bed boarding house, 80-bath radon therapy facility, 2 therapeutic pools and other resort units are under construction. A scientific research laboratory was organized at this resort, which is concerned with the mechanisms of effects and efficacy of radon therapy for cardiovascular, neurological and arthralgic diseases, as well as metabolic pathology. The resort is in close creative contact with scientists in the Siberian Department of the USSR Academy of Medical Sciences, Novosibirsk Medical Institute and Tomsk Scientific Research Institute of Balneology.

In addition to the Belokurikha and Chemal resorts, there are the following facilities in Altayskiy Kray: Lebyazh'ye tuberculosis resort, 700-bed Barnaul'skiy sanatorium, 2 boarding houses, 6 children's sanatoriums, 3 rest homes, mud bath facility (Bol'shoye Yarovoye Lake) with space for 150. There are plans for development of sanatorium and resort facilities in the steppe region of Altay also. More than 4000 lakes have been recorded there, most of which are salt and mud-containing lakes. Valuable therapeutic silt mud has been discovered in such lakes as Kulundinskoye, Kuchukskoye, Gor'koye-Komarinskoye, Gor'koye-Peresheychnoye, Shchelochnoye, Bol'shoye Zhirnoye, Mormyshanskoye and others. The stock of sulfide silt mud in Bol'shoye Yarovoye Lake alone constitutes more than 300,000 tons, with 264 million cubic meters of brine. The warm radioactive water of Kamen'-na-Obi, where a balneotherapy facility is under construction, mixed mineralized waters

in Romanovskiy, Zav'yalovskiy and Mamontovskiy Rayons, sulfate-chloride sodium and chloride-sulfate magnesium-sodium and calcium-sodium waters with 2-10 g/l minerals in Bayevskiy, Blagoveshchenskiy, Pankrushikhinskiy and Uglovskiy Rayons are promising for balneological purposes. In western Altay there are chloride sodium waters and brine. Some of these sources are on the records for construction of interkolkhoz and trade-union sanatoriums, mud baths and sanatorium-preventoriums of industrial enterprises.

The Kuznetsk Basin is also rich in natural therapeutic resources. In recent years, the mineral waters of the Kuznetsk Basin have been explored in Kemerovskaya Oblast. In the upper parts of the geological profile, there are nitrogen waters with complex chemical composition, with mineralization of 2.8-11.2 g/l at depths of 100-500 m and nitrogen-methane hydrocarbonate sodium waters with 2-5 g/l mineralization. Carbonate hydrocarbonate sodium and sodium-calcium waters are also encountered. It is planned to build a balneological 110-bed resort near the Mikar'yevskiy spring of carbonate water 75 km away from Novokuznetsk and this water (Tersinka water) is presently being bottled.

At the Borisovskiy spring of hydrocarbonate-chloride sodium mineral water, 100 km from Kemerovo, the first 500-bed section of a sanatorium complex is under construction, with plans for a second 100-bed section and bottling plant. Karachi type chloride-hydrocarbonate sodium water is found in the Kuznetsk Basin, Barzasskiy and other rayons. There is a stock of up to 1 million cubic meters of therapeutic mud in the large fresh-water lake, Bol'shoy Berchikul', in Tisul'skiy Rayon. There are deposits of peat suitable for therapeutic purposes. The 540-bed Prokop'yevskiy sanatorium, with boarding houses for 220 patients for treatment of nervous system and skeletomuscular diseases is near one of them. The sanatorium has modern mud and peat treatment facility, hydrotherapy facility with a shower department, physiotherapy and therapeutic physical culture departments. The 350-bed Anzherskiy sanatorium was opened in 1977 for treatment of patients with bronchopulmonary and cardiovascular diseases. There is a particularly broad network of children's sanatoriums (26), rest homes (7), sanatorium-preventoriums of industrial enterprises (69), local hiking and excursion centers in Kemerovskaya Oblast. In 1978, more than 76,000 people were treated and rested in sanatoriums and rest homes of the Kuznetsk Basin, more than 51,000 in Omskaya Oblast, 107,000 in Novosibirskaya Oblast and over 70,000 in Altayskiy Kray (not counting recreation and treatment of children).

The health resorts of Western Siberia and recreational areas have gained the deserved recognition of more than just local residents. Thousands of workers travel to Siberia for vacations, make use of the hiking trails in Altay, Baykal, Kamchatka and Sakhalin.

The sanatorium and resort network of Siberia is growing with each year; much is being done to upgrade medical care of the sick and vacationers, as well as to increase the efficacy of therapy. It is unquestionably urgent to make broader use of the natural therapeutic factors of Siberia to improve the health of the people. Like many social and cultural projects in Siberia, the construction of new and expansion of existing resorts, sanatoriums, rest homes, boarding houses and sanatorium-preventoriums should develop rapidly.

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CSO: 1840/192

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NATURAL THERAPEUTIC RESOURCES OF ISSYK-KUL' RESORT REGION, PROTECTION  
AND PROSPECTS OF DEVELOPMENT THEREOF

Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KUL'TURY  
in Russian No 2, Mar-Apr 81 (manuscript received 19 Jun 80) pp 10-14

[Article by D. A. Alymkulov, Kirghiz Scientific Research Institute of  
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[Text] Organization of sanatorium and resort therapy, as well as recreation  
for workers occupies an important place in the general plan of social develop-  
ment and health care of working people, as an important State measure that  
is being consistently implemented in our country. The Issyk-Kul' resort  
region, which was defined as a resort region of national importance by  
decision of the 25th CPSU Congress, can serve as an example of this.

The region of Lake Issyk-Kul' is characterized by a rare combination of natural  
factors--favorable climate with mountain and maritime features, various types  
of mineral water, large stock of therapeutic mud, excellent beaches and  
mountain landscapes of unique beauty.

The trough of Lake Issyk-Kul' is a unique region with respect to  
climate, due to its temperate latitude, intracontinental location  
in the desert zone of the temperate belt, isolation by the Kungey  
and Terskey Ala-Too mountain ranges; it is considerably south of  
Crimea. The clear skies mean that there is a long period of sun-  
shine and high intensity of solar radiations. Thus, the mean annual  
duration of sunshine on the shore of Issyk-Kul' constitutes 2670-  
2880 h, which is 400-600 h more than on the Black Sea coast of the  
Caucasus and Crimea. Biological activity of ultraviolet radi-  
ation is low in the winter (2-2.5 months/year) and high in the  
warm period (5.5-6.5 months). The significant elevation of the  
Issyk-Kul' trough [basin] above sea level (1607.5 m) and presence  
in the center of a deep nonfreezing lake with 6500 square meter  
surface influence formation of the climate.

An important distinction of the Issyk-Kul' region is also the minimal  
variability of meteorological factors: daily air temperature fluctua-  
tions constitute 0-2°C, atmospheric pressure changes constitute  
0-2 mbar and relative humidity is in the range of 0-10%. This makes

it easier to adapt to the environment, which is particularly important for patients with cardiovascular, bronchopulmonary and other diseases.

The staff of our institute have studied the climate (in April, July and October) for several years in various parts of the shores of Issyk-Kul', from the water's edge to the foothills of mountains along the ranges [lines?] of Chok-Tal, Bosteri, Sukhoy Khrebet and Kadzhi-Say. It was determined that lowest air temperatures in the summer are observed directly on the shore (10-20 m from the water's edge), and the temperature rises toward the mountains (by 0.5-1.0°C/km). The optimum relative humidity for man (60-70%) is also found on the shore, and it drops to 30-50% in the foothill plain. There is a steady, uniform breeze of 0.5-1.8 m/s along the shore, and the wind becomes intermittent toward the mountains, with velocity of 2-3 m/s (V. M. Fomin et al.).

There are 19 group therapeutic mineral springs concentrated in the territory of the Issyk-Kul' resort region (Table 1).

Most of the mineral sources of the Issyk-Kul' region are characterized by alkaline silicate hot springs (silicic acid 30-80 mg/l, fluorine up to 13 mg/l).

At the present time, the health resorts use Ak-Suu, Dzhergalan and Dzhetty-Oguz mineral water; in the near future they will use waters of the Cholpon-Ata group from mineral hot springs situated on the territory of the Ala-Too rest home, Goluboy Issyk-Kul', Cholpon-Ata, Issyk-Kul', Kazakhstan and other sanatoriums. Most of the mineral hot springs that are in use and still unused constitute the considerable resources of the Issyk-Kul' region.

The water of Issyk-Kul' Lake itself, which is used for baths extensively in some sanatoriums of this region, is of interest to the development of balneological sanatoriums and resorts. The therapeutic efficacy of such baths has been proven by the studies of the Kirghiz Scientific Research Institute of Balneology and Physiotherapy. The water contains 5.8-5.9 g/l minerals, and it has a chloride-sulfate sodium-magnesium composition. For several years, the staff of this institute has conducted studies for the purpose of preventing pollution of lake water.

Issyk-Kul'skiy Rayon is rich in mud. A total of 7 deposits of therapeutic mud with overall stock of over 2.5 million tons (Table 2) are concentrated in the waters and coastal parts of the lake.

However, the mud resources of Issyk-Kul' are not limited to the deposits that are known. Exploration revealed mud deposits in other parts of the Issyk-Kul' region.

The mud in this region is of a uniform type, and it is characterized as silty, bed-rock, sulfide, with low mineralization and sandy. It is plastic, black or dark brown with the odor of hydrogen sulfide. It contains no gypsum, has a specific mass of 1.4-1.8 and specific heat of 0.4-0.6 cal. The mud and mud solution have an alkaline reaction.

Table 1. Sources of mineral waters in the Issyk-Kul' resort region

Type of water	Source	Alt., m	Output, l/s	Temp., °C	Minerals g/l	Current use
Radon chloride sodium-calcium	Dzhety-Oguz	2200	4,5	23,6—38,5	0,7—13,0	Resort
Nitrogen silicic alkaline hot springs with low mineral content, of the Kul'dur type	Ak-Suu	1950	10,0	58,2	0,4	Sanatorium
	Chon-Kyzyl-Su	2410	1,5	25,6—40,2	0,4	Balneotherapy facility
	Bozuchuk	2200	0,6	29,0	0,9	--
	Dzhuukuchak	2800	0,6	32,8	0,4	--
	Keregetash	3040	0,2	46,0	0,9	Balneotherapy facility
	Altyn-Arashan	2335	0,4	50,5	0,4	--
	Sary-Dzhas	2519	Negli- gible	50,0	0,9	--
	Uch-Kaynar	1610	2,0	22,0	0,8	--
	Dzhergalan	1624	17,0	43,0	0,9	Resort
	Karabulun	1610	15,7	41,3	0,4	--
	Dolinka	1645	4,0	49,0	3,1	--
	Kurskoye	1645	8,3	42,0	0,9	--
Highly miner- alized chloride Na- Ca hot springs of Chartak type	Komsomol	1630	8,0 (p)	40,0	18,7	Exploration work completed
	Cholpon-Ata	1645	15—16 (p)	45—52	15—30	Stock con- firmed by
	Kirghiz Council of Ministers boarding house	1645	6,5(p)	48,5	15,0	GKZ Same
	Ala-Too	1640	8,0(p)	52	29,0	"
	Bozteri	1645	6,0(p)	45	40,0	Kazakhstan sanatorium
	Ulakhol	2450	—	16,0	1,3	--

Key: p) pumped out

GKZ) State Commission on Mineral Resources

Repeated studies and many years of experience have shown that Issyk-Kul' silt mud can recover its original therapeutic properties within 3-4 months and can be reused for up to 5-6 times (L. A. Khmyrova and P. I. Shogina, 1973).

A plan was developed for zoning of resorts over the entire territory of the Issyk-Kul' region, according to which the total capacity of the results should be brought up to 100,000 places by the year 2000, including 40,000 accommodations available the year round. For this purpose, it is planned to create 3 major subdistricts on the coastline, with 17 resort zones and 5 zones for brief vacations: northern with Cholpon-Ata as the center, eastern with Przheval'sk as the center and southern with Tamga as the center. There are plans for 4 resort zones with a total capacity of 48,000 places in the northern subdistrict, including 19,000 available the year round, 8 resort and therapeutic zones in the eastern one with 36,300 places, including 14,500 operating the year round and 4 therapeutic zones with a total capacity of 15,700 places in the southern one, including 6500 operating the year round.

At the present time, construction is in progress in the northern subregion, in accordance with approved general plans, on resort complexes in Cholpon-Ata, Dolinka, Bosteri, Kosh-Kul', as well as children's resorts in Kurskoye and Chok-Tal.

Table 2. Characteristics of therapeutic mud of Lake Issyk-Kul'

Deposit [source]	Re- source thous. tons	Den- sity g/cm <sup>3</sup>	Pol- luted by par- ticles 0.25 mm in di- amet., % dry mud	Total hydrogen sulfide, g/100 g mud	Current use
Chayka	7,0	1,6-1,8	1,1-1,6	0,113-0,268	Transported for use out- side of resort
Dolinka	7,4	1,4-1,7	4,7	0,131-0,157	Not used
Cholpon-Ata	26,1	1,3-1,6	1,3-2,9	0,099-0,667	Goluboy Issyk-Kul' sanatorium
Kurmenty	49,0	1,1-1,6	1,6-5,8	0,105-0,298	Not used
Dzhergalan	700,0	1,5-1,7	1,4-3,0	0,273-1,287	Dzhergalan resort
Pokrovka	1500,0	1,4-1,7	1,2-3,7	0,106-0,360	Not used
Tamga	40,0	1,4-1,7	5,9-8,2	0,003-0,157	Issyk-Kul' sanatorium

All this puts major problems to the institute. First of all, studies must be pursued of the effects on patients of the main climate elements in order to elaborate methods of "meteoprophylaxis."

Some work has already begun at low (Frunze), as well as moderate and high altitudes. The staff of the institute has been working for several years on indications and contraindications for treatment of patients in the Issyk-Kul' resort district. Thus, considering prevention of ischemic heart disease (IHD) as a social problem, they investigated the possibility of treating such cases at the resorts near Issyk-Kul'. There were patients with IHD and those with a risk factor for its development under observation. At the Cholpon-Ata resort, which is at moderate altitude, 94.5% of the patients were discharged presenting improvement and significant improvement. Long-term follow-up revealed that there was a 37% decrease in temporary disability following treatment at the resort. This made it possible to include the presence of risk factors for IHD and IHD with no more than grade I circulatory insufficiency among the indications for treatment at Issyk-Kul' resorts.

A team of institute personnel is concerned with rehabilitation therapy for patients with sequelae of simple skull trauma at sanatoriums of the Issyk-Kul' area at moderate and high altitudes, with the use of natural and preformed physical factors. The results were beneficial with treatment at the Cholpon-Ata resort (moderate altitude) in 91.4% of the cases and at the high-altitude resort of Dzhetty-Oguz in 96.9%, versus 88.9% when treated at the institute hospital (low altitude, 760 m above sea level).

Much work is being done, to implement the decisions of the 25th CPSU Congress, by the Central Committee of the Communist Party of Kirghizia and this republic's Council of Ministers with regard to developing resorts in the republic, making wise use of natural resources and environmental protection. Several decrees pertaining to these matters were adopted by the government of this republic in the last few years alone.

However, a number of new and complex problems arise, particularly with regard to preserving the region's natural resources, in view of the decline in level of Lake Issyk-Kul'. In many areas, the shoreline will shift 200-400 m from its present location, so that all resort buildings and improvements of the beach zone will be far from the water and away from the beaches. Moreover, the drop of the water level will cause irreversible changes in the microclimate, as well as loss of valuable natural therapeutic factors. Thus, a significant part of the sources of therapeutic mud of the Issyk-Kul' area is directly connected to lake water; without constant drainage of water into these sources, they will become buried under a layer of sand and they will lose their valuable therapeutic properties and biological activity.

As an example, we could mention the Tamga source of coastal mud, which no longer contains water due to the drop in its level. At the present time, this source is under a layer of sand and the mud is of a poor therapeutic quality. If the drop of lake water level will continue, this will also be the fate of therapeutic mud in other sources.

Of the entire beach zone, which is over 600 km long, Issyk-Kul' has more than 120 km of natural grade I and II beaches, including 30 km of children's beaches.

The decline in level of water in Issyk-Kul' will be associated with deepening of the coastal strip, which will have a particular effect on the children's resort zone, since the shallow beaches will disappear. Moreover, water temperature will drop by 4-6°C, since deep beaches will be left, where water warms up to 16°C in July and August, and this will shorten the swimming season. While visits to recreational institutions presently start in late May and last to the end of September, the interval will shift to the end of July up to the start of September with a drop in water temperature, i.e., it will decrease to two-thirds.

In other words, the drop of water level will lead to destruction of resort factors (these are virtually irretrievable losses, since the unique resort resources are entirely irreversible), and this will cause an enormous detriment to the national economy and public health, due to the curtailed period of going to sanatoriums, recreational institutions, Pioneer camps, etc. We deem it necessary to make every effort and take the most immediate steps to stabilize the water level in Issyk-Kul' Lake. Even now, one should proceed wisely and with concern in determining the fate of this lake, so that not only we, but our descendants will be able to make use of this priceless gift of nature.

In conclusion, let us stress that therapeutic mud and mineral water, together with the favorable climate factors, constitute a reliable foundation for developing climate and balneological, as well as mud, resorts in the region around Issyk-Kul'. However, it is imperative to take immediate steps to preserve the natural therapeutic resources of the lake in view of the decline of its water level.

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1981

10,657  
CSO: 1840/192



## PREDICTION OF COLLECTIVE RADIATION DOSES TO AES PERSONNEL

Moscow GIGIYENA I SANITARIYA in Russian No 2, Feb 82 (manuscript received 19 May 81) pp 40-42

[Article by M. S. Yegorova, A. M. Vorob'yev and G. M. Parkhomenko]

[Text] Forecasting estimates of collective doses are important to the safe operation of nuclear electric power plants (AES) and providing for a tendency to lower exposure of personnel.

The initial data for such estimates should be based on actual indicators for prior years of operation. For the sake of reliability, one must gather enough statistics on the initial indicators, using a more or less standardized approach for all types of AES. Such an approach should apply to the forms of keeping records of personnel exposure, using estimation coefficients (coefficient of power utilization, standard distribution, standard coefficient, normalized dose), making corrections for an aggregate of low doses on the level of sensitivity of the methods used, and others.

Lowering exposure of AES personnel is related to many diverse technical and organizational factors: quality of fuel elements and reliability of circuit equipment, choice of building materials, quality of biological protection, purification of heat carrier [cooling agent], accessibility of equipment to repairs, proper organization of all work and qualifications of personnel. Well-organized monitoring and records of doses involved in different operations presenting a radiation hazard plays a large part. It helps detect the areas of work related to maximum doses so that one could devote attention to expressly these operations in the future. The doses ["dose inputs"], when determined reliably on extensive material for the different operations, help the AES management not only in planning dose inputs for proposed overhaul, but in setting them in plans for new AES.

Table 1 illustrates an example of the form of recording dose input.

The collective dose is found by adding individual doses measured with disposable dosimeters (KID-6A) or, as a last resort, by multiplying the average dose rate by work time.

Table 1. Form for recording exposure of AES personnel while conducting work presenting a radiation hazard

AES sector	Type of work	Number of people	Labor, man-hours	Collective dose, man-rem	Remarks
Reactor shop, lower water-communication rooms	Replacement of water-flow regulators ("shadry" [?])	50	1000	10	Replacement of 500 "shadry"
Centralized overhaul shop	Inspection and repair of drum separator	30	300	5	Adverse meteorological conditions, 50°C temperature
Electric shop, machine shop	Laying cable	4	50	0.1	
Totals		84	1350	15.1	

It is recommended to keep a record of dose inputs on this form during both the period of normal operation and during capital and scheduled preventive overhaul and elimination of consequences of accidents.

At the present time, keeping records of actual dose inputs has not been sufficiently organized. It would be meaningful to indicate in proposed design materials not only the overall collective dose related to overhaul and normal operation, but the "quotas" for servicing specific types of equipment. For this reason, the dosimetric monitoring service is faced with the task of automating these estimates, taking advantage of the possibility of inputting and systematizing the data on individual dosimetric monitoring in a computer. It would be desirable to institute a radiation-dosimetry record card file for each type of equipment, including such information as how long it has been in operation, interval between two successive overhauls, time spent on each overhal and collective dose per routine overhaul.

For AES with VVER-440 [water-moderated, water-cooled power reactor], one should single out such equipment as reactor housing, units inside the housing, main circulation pumps, main lock gates, steam generators, volume compensators, pipes in the first contour [?] and DU-500 nozzles [connecting pipes]; for AES with RBMK-1000 this refers to the main circulation pumps, drum separators, ball governors of water flow, locking and adjusting valves, etc.

According to the latest recommendations of the ICRP [International Commission on Radiological Protection], a dosage of 5 rem should be allowed only in a few cases as the maximum level of irradiation, whereas for all those working with sources of ionizing radiation, the exposure dosage should be an average of one-tenth less. This recommendation will be feasible if the distribution

of individual doses is planned in advance not to exceed the standard distribution (NKDAR [expansion unknown] report). The logarithmically normal distribution, for which the mean dosage will be 0.5 rem and the percentage of people exposed to above the maximum permissible doses (MPD) is limited to 0.1, is taken as the standard. The Figure illustrates such distribution schematically. The cross-hatched segment after 5 rem shows the relative share of indicators exceeding 5 rem. For standard distribution selected in this manner there is another inherent condition: the ratio of collective dose to personnel exposed to annual doses in excess of 1.5 rem ( $S_{>1.5}$ ) to the entire collective dose ( $S_{\infty}$ ) will constitute 0.31. This ratio may have the following appearance:

$$\left( \frac{S_{>1.5}}{S_{\infty}} \right)_{\text{standard}} = 0.31.$$

The actual distribution of individual doses may differ appreciable from the standard, but in any case it can be described by two parameters: mean dose  $\bar{D}$  and standard coefficient  $\Omega$ . The latter will be the quotient of two ratios: in the numerator--ratio of collective dose formed of individual doses in excess of 1.5 rem to entire collective dose for the distribution analyzed, in the denominator--the same ratio for the selected standard distribution:

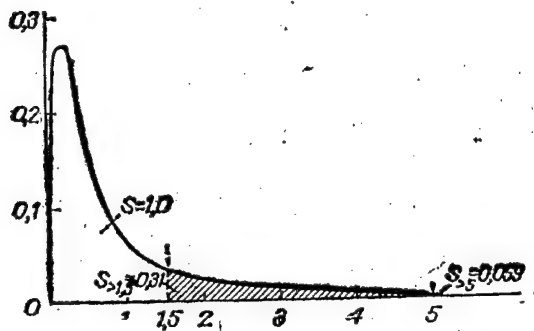
$$\Omega = \frac{\left( \frac{S_{>1.5}}{S_{\infty}} \right)_{\text{act.}}}{\left( \frac{S_{>1.5}}{S_{\infty}} \right)_{\text{standard}}} = 3.23 \left( \frac{S_{>1.5}}{S_{\infty}} \right)_{\text{actual}}$$

For a standard distribution,  $\Omega = 1$ ; the more  $\Omega$  deviates from 1 to 3.23, the greater the fear that there will be an appreciable rise in percentage of individual doses exceeding 1.5 rem and those approaching 5 rem. We illustrate this in Table 2.

Table 2. Characteristics of real distributions

Conventional shop No	Collective dose (S), man·rem	Collective dose, man·rem with levels of >1.5 rem ( $S_{>1.5}$ )	Mean dose ( $\bar{D}$ ) rem	Standard coefficient ( $\Omega$ )	Characteristics of standard distribution	
					$\bar{D}$	$\Omega$
1	595	300	1.07	1.6	0.5	1
2	94	40	0.97	1.38	0.5	1
3	25	0	0.13	0	0.5	1
4	47	14	0.49	0.97	0.5	1
5	65	65	4.08	3.23	0.5	1
6	396	220	2.12	1.8	0.5	1

Unfortunately, these two features do not enable us to determine the percentage of individuals exposed to more than 5 rem, but they do give us a rather objective idea about the greater or lesser probability of being exposed to a dose in excess of 5 rem. Table 2 shows that the possibility of doses in excess of 5 rem is ruled out in distributions 3 and 4, whereas in the others this probability is other than zero, and it is highest in distribution 5.



Standard logarithmically normal distribution of individual annual doses of radiation

Mean dose  $\bar{D} = 0.5$  rem; median  $\xi = 0.345$  rem; standard geometric deviation  $\sigma_g = 2.38$ ; probability of receiving in excess of 5 rem  $P_{>5} = 0.1\%$ . X-axis, range of doses (rem); y-axis, frequency of individual doses in indicated range

Experience in operating foreign and Soviet AES (Yu. V. Sivintsev; A. I. Burnazyan) has shown that working conditions for AES personnel may be considered good with no danger of over-exposure, provided radiation safety standards and sanitary rules are followed. Many years of observations made it possible to estimate the most representative parameters, such as mean individual doses to AES personnel (rem/year), collective dose to all personnel (man·rem), standardized dose per unit electric energy produced [man·rem/mW(el.)·year], as well as percentile contributions to the collective dose of doses referable to normal AES operation and repair work.

Having summed up the accumulated information, we can use it as the basis for estimating typical parameters in

future AES. In particular, the standardized collective dose per unit of produced energy constitutes about 1.1 man·rem/gW×(el.)·year for Soviet AES with VVER-440 reactor and foreign AES (Yu. V. Sivintsev; Yu. E. Khandamirov) with PWR reactor. Taking 70% as the capacity factor (CF), one can estimate the collective dose for operation of one AES unit with VVER-440 reactor at 340 man·rem. Proceeding from this, one can assess the "quotas" for normal operation and repairs. For PWR and VVER-440 reactors (Yu. V. Sivintsev, Yu. E. Khandamirov), 62-66% of the collective radiation dose is referable to repair work. Consequently, exposure of personnel during the period of normal operation should be in the collective dose range of 120-130 man·rem/year, while the remaining 210-220 man·rem can be planned for repairs.

Let us make an analogous calculation for AES with RBMK-1000 reactor. If the standardized collective dose is taken as 1.2 man·rem/gW/(el.)·year and CF as 70%, the collective dose will be 840 man·rem. Repair work on the RBMK-1000 constitutes 32%, i.e., the "quota" for repairs will be about 270 man·rem and one should set 570 man·rem for normal operating work.

According to data covering 27 reactor-years, the mean data revealed that the doses were on the level of 1/10 of the MPD, i.e., 0.5 rem. One can determine the minimal number of personnel for typical AES on the basis of these and the above-estimated parameters.

For stations that are at the planning stage, it is recommended that the limit of specific (standardized) dose of 0.2 man·rem/gW(el.)·year be used (O. S. Bazykin). This limit leads to collective radiation doses of 60-65 man·rem for personnel of VVER-440 and about 140 man·rem for RBMK-1000.

The estimates discussed here pertain only to external gamma radiation, the recording of which is regularly refined. Major practical difficulties arise with regard to predicting internal radiation to AES personnel. Of course, the dosage thereof will be low; however, it should also be specified in planning materials to have a complete set of data.

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10,657  
CSO: 1840/203

COMPETITION BETWEEN ALGAE IN FLOWING SYSTEM

Moscow ZHURNAL OBSHCHEY BIOLOGII in Russian Vol 43, No 2, Mar-Apr 82  
(manuscript received 17 Jan 80) pp 205-211

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[Abstract] Using a simple model as an example, the authors established the relationship between flowing and closed systems and analyzed the qualitative nature of the transient process in an open ecosystem based on knowledge of the structure of steady states of a closed system. The analysis was based on a model of competition of two freshwater Diatomeae alga species (*Asterionella formosa* Hass. and *Cyclotella meneghiana* Kutz.) for components of nutrition. The results of the study of phytoplankton communities in both closed and open flowing systems were used to explain the experiments on algae competition over long periods of time. The boundary between domination of *Cyclotella m* and the existence of two species is modeled with good accuracy by the mathematical equations developed in this article, properly describing both the location and the shape of areas of stable results of the competition. Figures 2; references 5: 4 Russian, 1 Western.  
[243-6508]

INTERACTION OF OPIATES AND OPIOID PEPTIDES WITH BRAIN MEDIATOR SYSTEMS

Moscow USPEKHI FIZIOLOGICHESKIKH NAUK in Russian Vol 13, No 2, Apr-Jun 82  
pp 65-92

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[Abstract] This review of the [primarily American] literature studies the interaction of opiates and opioid peptides with various mediator systems in the central and peripheral nervous system. These substances influence the synthesis, liberation, conversion and utilization of acetylcholine in the central nervous system. Noradrenalin also participates in the analgesic effect of morphine. The literature indicates the existence of a relationship between the opiates, including enkephalins and endorphins, and dopaminergic structures in the brain. Some reports also indicate participation of serotonergic mechanisms in the analgesic effect of the opiates. Pain stimulus results in an increase in the content of gamma-aminobutyric acid in the gray matter, cerebral cortex, hypothalamus and reticular formation. Finally, histamine has been demonstrated to be a mediator in the peripheral and central nervous system. Common links are sought in the action of opiates and mediators, and may include the cyclic nucleotides, which transmit the effect of mediators to a neuron and change various intraneuronal processes. The opiates influence the content of cAMP in the brain. The change in cAMP and cAMP content represents a significant part of the mechanism by which opiates and opioid peptides act on the central and peripheral nervous systems. Other common components in the mechanisms of action of mediators, opiates and opioid peptides are the prostaglandins and calcium ions. References 249: 15 Russian, 234 Western.  
[223-6508]

PHYSIOLOGY

UDC: 612.822.1+612.825+612.826

NEURON MECHANISMS OF HYPOTHALAMUS-RETICULAR INFLUENCE ON CEREBRAL CORTEX  
ACTIVITY

Moscow USPEKHI FIZIOLOGICHESKIKH NAUK in Russian Vol 13, No 2, Apr-Jun 82  
pp 3-30

BAKLAVADZHYAN, O. G. and YEGANOVA, V. S., Institute of Physiology imeni  
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[Abstract] This review of the Soviet and American literature outlines the structural and functional organization of hypothalamus-cortical and reticulo-cortical interactions, plus neuron organization of hypothalamus-reticular interactions. The hypothalamus is looked upon as a pacemaker center which plays a decisive role in the formation of basic biological motivations as one of the primary regulators of homeostasis of cortical excitation. Direct projection of the hypothalamus into various cortical formations has been demonstrated. The multichannel ascending hypothalamus-cortical system consisting of both activating and inhibiting subsystems plays an important role in regulation of functions such as sleep and waking, digestion, the cardiovascular system, the endocrine system and temperature regulation. An extensive electrophysiological literature is cited, studying the ascending activating influence of the midbrain reticular formation on neocortex activity. The existence of direct connections of various cerebral cortex areas with all brain stem reticular formation areas has been convincingly proven. Hypothalamus-reticular interactions are also important in the mechanism of functioning of the hypothalamus-cortical and reticular-cortical integration systems. Most electrophysiological studies have confirmed the direct projection of the ascending afferents of the midbrain reticular formation in the structures of the rostral hypothalamus. Further development of hypothalamus-cortical interaction problems is important and promising for determination of the functional organization of associative cortical zones and mechanisms of integrative activity of the hypothalamus. Figures 3; references 184: 65 Russian, 119 Western.

[223-6508]



## DYNAMICS OF MINUTE WAVES IN INFRASLOW BRAIN ACTIVITY IN VARIOUS METHODS OF ELECTRICAL STIMULATION OF TWO ZONES IN NEOCORTEX

Leningrad FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I. M. SECHENOVA in Russian Vol 68, No 3, Mar 82 (manuscript received 13 Feb 81) pp 303-310

BORODKIN, Yu. S., LAPINA, I. A. and GOGOLITSYN, Yu. L., Department of Pharmacology of Memory and Behavior and Department of Human Neurophysiology, Institute of Experimental Medicine, USSR Academy of Medical Sciences, Leningrad

[Abstract] Many researchers consider that infraslow cerebral wave activity reflects the metabolic level in neuron populations, offering a criterion on which to assess stabilization or restructuring of neural metabolism as seen in the pattern of mean values for wave amplitude. Infraslow cerebral activity is also thought to play a role in insuring memory processes. Long-term experiments were conducted on 9 rabbits with indwelling electrodes in the frontal neocortical area in the field of the prefrontal gyrus, in the motor neocortex field 4, and in the dorsal hippocampus field CA-3. Electrical stimulation at 2.5-3.0  $\mu$ A was applied sequentially to the fields, causing no significant change in the 1/10 sec. and minute waves, and simultaneously to all fields or combinations of two fields, which resulted in significant shifts in wave activity. Artificial stable functional links set up by simultaneous stimulation of two areas or all areas were prolonged by the administration of the neurotropic agent aethimizol for up to 2 weeks; the shortened reflex was affected for up to 1 week. It is suggested that the differing patterns in slow-wave shifts can be explained by the nature of the artificial stable functional links and shortened reflexes established between different parts of the brain as seen in the metabolic effects. Figures 4; references 18: 16 Russian, 2 Western.  
[191-9642]

## SPATIAL HEARING: LOCALIZATION OF STATIONARY AND MOVING SOURCES OF SOUND

Moscow USPEKHI FIZIOLOGICHESKIKH NAUK in Russian Vol 12, No 4, Oct-Dec 81  
pp 28-51

AL'TMAN, Ya. A., Institute of Physiology imeni I. P. Pavlov, USSR Academy of  
Medical Sciences, Leningrad

[Abstract] This article reviews work done to characterize the main patterns in spatial auditory perception of sound from stationary and moving sources. The following aspects are discussed: auditory perception in man of sound from stationary and moving sources, including determination of spatial position of the sound source in the horizontal plane, determination of the distance to a sound source, and determination of the angle of rise from a sound source; localization of stationary and moving sources of sound in impaired activity of the central sections of the system of hearing, including animal experiments and studies on human patients; electrophysiological studies on the mechanisms on localization of stationary and moving sounds. Figures 6; references 76: 28 Russian, 48 Western.  
[199-9642]

UDC 612.821.6 + 575.42

CAPACITY FOR LEARNING AND EXTRAPOLATION IN MICE SELECTED FOR DIFFERENT  
BRAIN WEIGHT

Moscow ZHURNAL VYSSHEY NERVNOY DEYATEL'NOSTI IMENI I. P. PAVLOVA in Russian  
Vol 31, No 3, May-Jun 81 (manuscript received 8 Apr 80) pp 550-555

POPOVA, N. V., POLETAYEV, I. I. and ROMANOVA, L. G., Department of Physiology  
of Higher Nervous Activity, Moscow State University imeni M. V. Lomonosov

[Abstract] A comparative study was made on the F13-15 generations of two sub-lines of mice selected for large (L) (36) and small (S) (34) brain-versus-body weight in order to determine relative levels of learning (a simple food reflex) and extrapolation behavior (determining the direction of a straight-line shift in a food stimulus with the food not visible to the animal) and the degree to which learning patterns are retained. The findings were as follows: L mice learned a simple food-search response more rapidly than S mice, and L mice continued to learn more rapidly than S mice; in the extrapolation study, the 50% random level from an alternative choice was seen in the first presentation of the situation, and in further presentations the percentage of correct solutions increased and mean performance time decreased but no differences were

found between L and S subjects. Since this is the first time that this experiment has been conducted it would be premature to conclude that the differences found are the result of the different brain sizes; the experiment would have to be repeated in order to eliminate the possibility of random matching of these signs. Figures 2; references 9: 4 Russian, 5 Western.  
[201-9642]

BIOACOUSTIC CHARACTERISTICS OF SONAR SYSTEM IN EUROPEAN BAT  
(BARBASTELLA BARBASTELLA)

Moscow BIOFIZIKA in Russian Vol 26, No 6, Nov-Dec 81  
(manuscript received 18 Nov 80) pp 1090-1095

KONSTANTINOV, A. I. and MAKAROV, A. K., Leningrad State University imeni  
A. A. Zhdanov

[Abstract] The European bat *Barbastella barbastella* was selected for a quantitative evaluation of its sonar system in view of the unique signals that it emits and the size and configuration of the pinnae. The results showed that frequency-modulated signals, 1.8-2.5 msec in duration, are emitted by this species. The two frequency components showed a linear fall in the frequency from the beginning to the end of emission in the 56-23 kHz and the 80-55 kHz bands. Most of the signal energy is concentrated in the 23-35 and 60-75 kHz bands. Frequency-threshold curves revealed two low-threshold regions of perception, one with a minimum threshold of 0 dB at 20-35 kHz, and the other with 17 dB at 60-65 kHz. Evaluation of the evoked potentials in the posterior corpora quadrigemina showed that the threshold duration of a signal for a response was 0.7 msec, with a maximum evoked response occurring to 200-300 impulses/sec. Determinations of the optimal horizontal and vertical planes of the pinnae for signal perception at the two emitted frequencies and loss of sensitivity (in dB/degree) on deviation from the optimal spatial positions indicated that target position can be determined with an accuracy of 2-3°. This was attributed to the fact that maximum auditory sensitivity coincided with the most significant frequencies of the emitted signals, leading to optimum filtration of the incoming echoes and greater efficiency of this particular biosonar system. Figures 3; references 17: 4 Western, 13 Russian.  
[248-A-12172]

## DOMINANT AND ITS SIGNIFICANCE IN ANIMAL BEHAVIOR

Moscow USPEKHI FIZIOLOGICHESKIKH NAUK in Russian Vol 13, No 2, Apr-Jun 82  
pp 31-47

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USSR Academy of Sciences, Moscow

[Abstract] The dominant phenomenon was first observed in 1881 by Vvedenskiy, in a study of the influence of electrical stimulation of the vagus nerve on animal respiration. The dominant was later explained as a general principle of operation of nerve centers, the basis of constant restructuring of relationships among centers. The dominant focus of excitation determines the nature of nerve center reactions at a given moment. A stable focus of elevated excitation, no matter what it is evoked by, causes additional excitations to serve only as reinforcement or confirmation of excitation in the focus with widespread inhibition in the remaining portion of the central nervous system. Ukhtomskiy thus defined the dominant focus of excitation as one characterized by increased excitability, persistence of excitation, summation and inertia. Western authors, while not mentioning the dominant phenomenon, note that, for example, a hungry person perceives indefinite or imaginary stimuli as associated with food. Following the stage of summation, a reflex act is generated by the dominant which results in resolution of the dominant. The results which have been obtained to date indicate that the stage of resolution of the dominant serves as a basis for rapid formation of a firm time correlation between centers in which the dominant focus has arisen and centers to which the stimulus is addressed. It is the stage of completion of the dominant which is the basis for the expedient reaction of the animal and behavioral forms which resolve the dominant. Figures 3; references 41: 34 Russian, 7 Western.  
[223-6508]

UDC: 591.111.3

## NERVOUS REGULATION OF BLOOD LIQUID STATUS AND COAGULATION

Moscow USPEKHI FIZIOLOGICHESKIKH NAUK in Russian Vol 13, No 2, Apr-Jun 82  
pp 93-122

KALISHEVSKAYA, T. M. and GOLUBEVA, M. G., Moscow State University imeni  
M. V. Lomonosov

[Abstract] This review of the Soviet and American literature outlines modern concepts of the mechanisms of preservation of the liquid state of the circulating blood and possible causes of intravascular coagulation. The nature

and function of the anticoagulant system, its humoral agents and their significance in preservation of the blood as a liquid are outlined, as well as basic concepts concerning physiological regulation of a coagulant and anticoagulant system of the blood. The significance of interoreceptors in the vascular bed as a part of nervous and humoral regulation of the blood anticoagulant system is discussed as is the participation of the central brain formations in the regulation of blood coagulation. The significance of the autonomic nervous system in regulating the liquid state of the blood and its coagulation is described. The many experimental and clinical studies summarized here indicate that the mechanism of blood coagulation is regulated by the sympathetic and parasympathetic segments of the autonomic nervous system. Stimulation of the sympathetic nervous system stimulates thrombinogenesis, while the appearance of excess thrombin in the blood operates through the chemoreceptors in the vascular bed to activate the anticoagulant system by activating the parasympathetic segment of the autonomic nervous system. The liberation of anticoagulants and fibrinolytics in turn leads to excitation of the sympathetic segment of the autonomic nervous system. References 160: 102 Russian, 58 Western.

[223-6508]

UDC: 616:152.21-02:615.849.1]-07-092.9

ATTENUATION OF RADIOPROTECTIVE EFFECTS OF ACUTE HYPOXIA ON ANIMALS ADAPTED TO HIGH ALTITUDES

Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 27, No 3, Mar 82  
(manuscript received 4 Nov 81) pp 60-62

[Article by P. Kazymbetov, Alma-Ata Medical Institute]

[Text] It has been established that the radioprotective effect of acute hypoxia (5-6% oxygen) depends on time prior to irradiation that it is used (V. M. Krimker et al.; S. P. Yarmonenko and I. M. Epshteyn). When animals are kept for a long time in a pressure chamber at low pressure or with prolonged inhalation of hypoxic gas mixtures prior to irradiation, it was demonstrated that the radioprotective effect of brief acute hypoxia is diminished (V. G. Ovakimov and S. P. Yarmonenko; Yarmonenko et al.). Our objective here was to investigate the range of modification of radiosensitivity by acute hypoxia (6% oxygen) in animals adapted to high altitudes.\*

Experiments were conducted on mongrel white rats weighing 150-200 g and mice weighing 18-24 g, which were kept at the Institute's vivarium (control) and the Tyan'-Shan' Station at an altitude of 3340 m above sea level. Partial oxygen pressure in the air at the level of this station is 25% lower than in Alma-Ata, which constitutes about 15% oxygen in inhaled air. After 40-day adaptation at the station, the animals were returned to the city and, on the same day, exposed to x-radiation from an RUM-17 unit under the following conditions: 15 mA, 200 kV, focus to skin distance 30 cm, dose rate 2.44 Gy/min.

The hypoxic mixture containing 6% oxygen was prepared by the method of I. Yu. Kir'yanov et al., by mixing air with nitrogen gas using the Narkon-P anesthesia machine; A GK-1 gas analyzer was used to monitor oxygen content in the mixture. The animals were irradiated in plexiglas boxes 15×15×10 cm in size for rats and 15×15×6 for mice. The boxes with control animals had small windows on three sides and, for irradiation under hypoxic conditions, they were airtight, having two ducts, one of which was used to deliver the hypoxic mixture from previously filled Douglas bags 2 min before and during irradiation.

Animal survival for 30 days after irradiation and quantity of bone marrow cells in one thigh by the method of Ye. N. Kabakova et al. on the 3d

\*The author thanks Prof S. P. Yarmonenko for suggesting the topic and his assistance.

postradiation day served as criteria of radiosensitivity. In a separate series of experiments, we tested the toxicity of acute hypoxia for control and adapted animals. There were 10 to 20 animals per point for consideration of survival and 5-6 for counting bone marrow cells.

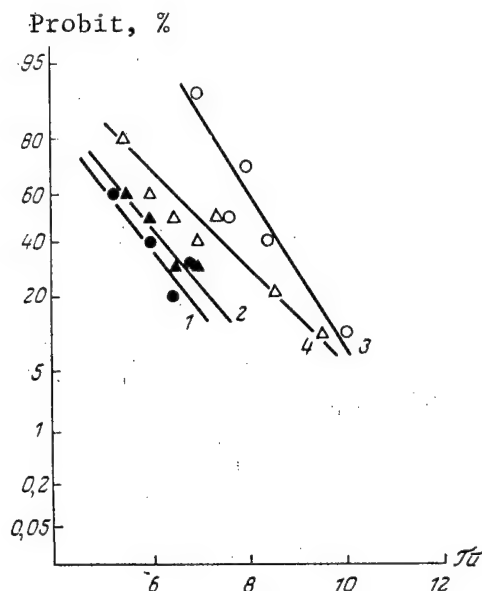


Figure 1.

Survival of intact and hypoxia-adapted rats irradiated under acute hypoxic conditions (5% oxygen). Here and in Figures 2 and 3:

- 1) irradiation of intact rats in air
- 2) irradiation of adapted rats in air
- 3) irradiation of intact hypoxic rats
- 4) irradiation of adapted hypoxic rats

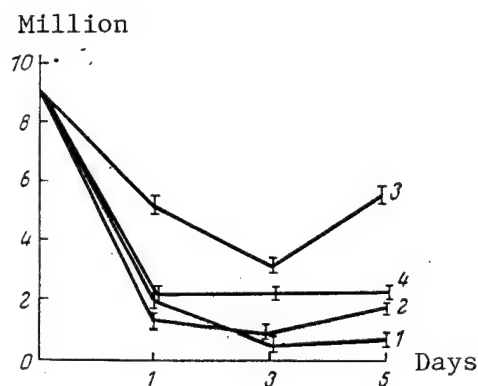


Figure 2.

Change in total bone marrow cells in intact and hypoxia-adapted rats irradiated under acute hypoxic conditions (6% oxygen)

#### Toxicity of acute hypoxia for intact and altitude-adapted mice

Oxygen content in gas mixture, %	Animal group	Number of animals	Survivals, %	Mean survival time, min (M±m)
5	Intact	12	58.3	8.4±4.0
	Adapted	10	100	
4	Intact	10	0	3.3±0.6
	Adapted	10	50	8.1±5.1
3	Intact	10	0	1.5±0.5
	Adapted	10	0	3.5±0.6
2	Intact	10	0	1.16±0.2
	Adapted	10	0	2.2±0.1

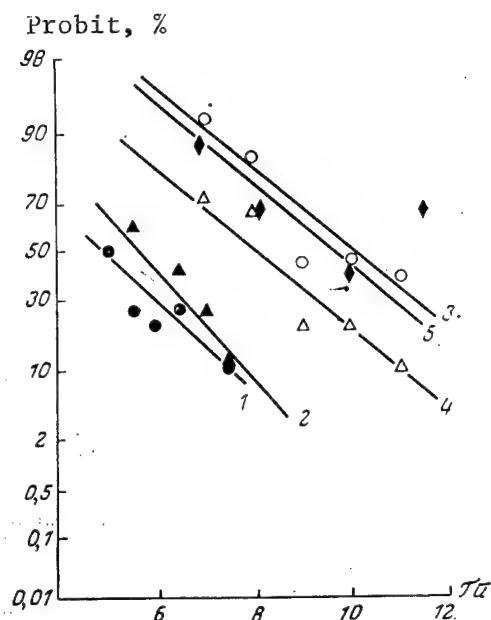


Figure 3.  
Survival of intact and altitude-adapted mice irradiated under acute hypoxic conditions (6% oxygen).

- 5) irradiation of adapted mice under hypoxic conditions on 10th day of deadaptation period

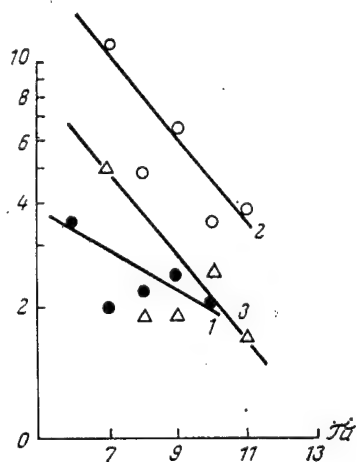


Figure 4.  
Change in number of bone marrow cells in intact and altitude-adapted mice  
1) irradiation of intact mice in open air  
2) same under hypoxic conditions  
3) irradiation of adapted mice under hypoxic conditions

When rats were irradiated 2 min after exposure to the hypoxic gas mixture, the dose reduction factor (DRF), measured from the ratio of  $LD_{50}$  for control and adapted rats, constituted 1.5 and 1.2, respectively (Figure 1), i.e., the radioprotective effect of acute hypoxia was diminished in the adapted animals. Adaptation per se lowered radiosensitivity insignificantly.

Attenuation of the radioprotective effect of acute hypoxia in animals adapted to high altitudes was also demonstrated by the indicators of damage to hemopoietic cells and, as can be seen in Figure 2, there were fewer bone marrow cells in adapted animals than intact ones for the first 5 days after irradiation under hypoxic conditions.

The decrease in radioprotective effect of acute hypoxia on adapted animals was also confirmed in experiments on mice. As can be seen in Figure 3, DRF constituted 2.0 and 1.6 for control and adapted mice, respectively, which were irradiated under hypoxic conditions. As shown by our subsequent studies, the adaptation effect was virtually removed 10 days after descending from the mountains; by this time, DRF constituted 1.9, i.e., it was close to the level of control animals.

Figure 4 illustrates the changes in total number of bone marrow cells in control mice and those adapted to altitude hypoxia irradiated under acute hypoxic conditions. We see that there were much fewer cells in adapted animals than the controls.

A special series of studies was conducted in order to determine toxicity of acute hypoxia for intact and adapted animals. As shown by the results of this study, adapted animals were twice as resistant to acute hypoxia as control animals, as shown by the survival rate and mean survival time of animals that expired (see Table).



Thus, as a supplement to previous studies, in which attenuation of the radio-protective effects of acute hypoxia was demonstrated in animals adapted to hypoxia under artificial conditions, in these experiments adaptation occurred under natural conditions for a rather long period of time. It was found that animals adapted to the mountains for 40 days presented attenuation of the radio-protective effect of acute hypoxia. Moreover, it was demonstrated for the first time that the diminished effect of acute hypoxia persists for several days after descending from the mountains. Perhaps, the less marked radio-protective effect of acute hypoxia observed in intact animals, as compared to data in the literature, is related to the fact that Alma-Ata is situated 800 m above sea level and that consequently there was slight hypoxia.

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CSO: 1840/189

CYTOGENETIC ANALYSIS OF PERIPHERAL BLOOD LYMPHOCYTES OF INDIVIDUALS EXPOSED TO LOW DOSES OF IONIZING RADIATION

Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 27, No 3, Mar 82  
(manuscript received 8 Jun 81) pp 70-72

[Article by S. P. Petrova]

[Text] There is a significant number of works dealing with the problem of assessing the chronic effects on man of low doses of ionizing radiation. However, analysis of the results of these studies does not enable us to arrive at an unequivocal conclusion, because of their great contradictions. According to some authors (A. V. Sevan'kayev et al.; S. T. Zhivkov et al.; Bocian and Ziemba-Zak; Donev et al.; Forni et al.; Popescu and Stefanescu; Visfeldt; Wald and Koizumi), the incidence of chromosomal aberrations is considerably above the spontaneous level in individuals exposed to low doses of ionizing radiation for a long time. Conversely, other researchers (M. N. Gorizontova and V. B. Khvatov; Anger and Jacobson; Court Brown et al.; Depenbusch) found no reliable increase in chromosomal aberrations.

Our objective here was to determine whether there is an increase in incidence of chromosomal aberrations in peripheral blood lymphocytes of individuals exposed for long periods of time to external gamma radiation.

Material and Methods

We analyzed the peripheral blood of 30 men 29-44 years of age, who had been exposed to external gamma radiation for 4-17 years. The annual radiation doses were in the range of 0.5-20.0 mSv.\* Cumulative radiation doses for the entire period of work constituted 10-200 mSv. The control group consisted of 20 men 24-55 years of age, who had not been exposed previously to ionizing radiation, except for routine diagnostic purposes. We failed to demonstrate appreciable deviations from normal in concurrent clinical studies of subjects in the main and control groups. All were deemed to be essentially in good health. Peripheral blood was cultured by the conventional method (Moorhead et al.), using Eagle medium and Reanal (Hungary) phytohemagglutinin. Cultivation time was 52 h. Colchicine was added 3 h before fixation in a concentration of 0.5 µg/ml. Hypotonic treatment was performed with 0.55% potassium chloride

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\*Translator's note: Sv stands for Sievert (Rolf Sievert), a unit named after the Swedish specialist in radiation protection, equivalent to 1 J/kg or 10<sup>2</sup> rem.

at 37°C in an incubator for 8 min. The cells were fixed in a mixture of methanol and glacial acetic acid (3:1); specimens were prepared by the method of burning out the fixing agent and stained according to Giemsa. In each case, we analyzed 100 metaphase plates with at least 44 and no more than 47 chromosomes. We took into consideration all aberrations encountered of the chromosomal and chromatid types. Deletions were not classified as aberrations. The data were submitted to statistical processing by the method of Fisher for estimating difference in sample shares (N. A. Plokhinskiy).

## Results and Discussion

Table 1 lists the results of our study. In the main group, we found 0.67 aberrations of the chromosome type per 100 cells and 0.35 in the control. The difference is statistically unreliable ( $P > 0.05$ ). Incidence of chromatid aberrations per 100 cells in the main group (0.47) did not differ appreciably from the spontaneous level (0.35). Single and paired fragments were the main types of aberrations demonstrated in both groups. The incidence of aneuploid cells was reliably higher in the main group (4.36%) than in the control (2.6%). The increase in number of aneuploid cells was due to hypoploid cells. The incidence of hyperploid cells did not increase (0.23% in the main group and 0.20% in the control). To analyze the dose-effect function, we divided the main group into three subgroups, according to cumulative dose: first subgroup--10-30 mSv; second subgroup--31-50 mSv; third subgroup--51-200 mSv (Table 2). We failed to demonstrate significant differences between subgroups with respect to incidence of chromosome aberrations per 100 cells, chromatic aberrations per 100 cells or quantity of aneuploid cells.

Thus, our findings revealed that there was no appreciable change in incidence of structural aberrations in peripheral blood lymphocytes with chronic exposure to radiation in doses of less than 20 mSv/year for 4-17 years, as compared to the spontaneous level. There were twice as many aneuploid cells in the main group as in the control. The increase in aneuploidy is attributable to hypoploid cells. The incidence of hyperploid cells did not change. Evidently, the demonstrated hypoploidy is not real, and it is due to loss of chromosomes in the course of preparation of the specimens. This could be related to radiation-induced change in lymphocyte sensitivity to hypotonic solution and decrease in their resistance (M. N. Gorizontova and V. B. Khvatov). Our results conform well with the data in a number of publications (M. N. Gorizontova and V. B. Khvatov; Anger and Jacobson; Brown et al.; Brown and McNeil; Depenbusch). Thus, M. N. Gorizontova and V. B. Khvatov, who used gamma-neutron radiation in doses of less than 50 mSv/year and cumulative dose of external radiation of  $128 \pm 28$  mSv for 10-12 years, failed to demonstrate changes in incidence of chromosome aberrations, as compared to the spontaneous level. The incidence of aneuploid cells was reliably increased. Brown et al., who used gamma radiation in doses of 77-360 mSv for 7-15 years and gamma-neutron radiation in doses of 43-159 mSv for 4-12 years, failed to find an increase in overall frequency of chromosome aberrations or aneuploid cells, as compared to the control. Nevertheless, the incidence of dicentrics was higher (0.5%) in the main group than the control (0.1%). Brown et al., using chronic gamma radiation for 5-15 years (cumulative doses 10-90 mSv) failed to demonstrate a reliable increase in incidence of stable and unstable aberrations, but with larger doses over a period of 15 years, a reliable increase was found in incidence of

Table 1. Incidence of chromosomal aberrations and aneuploid cells in culture of peripheral blood leukocytes for subjects in the main and control groups

Group	Number of subjects	Total metaphases analyzed	Aberrations (per 100 cells)		Structural aberrations (per 100 cells)	Cells (%) with		Total aneuploid cells, %
			chromosome	chromatid		44-45 chromosomes	47	
Main	30	3000	0.67	0.47	1.14	4.13	0.23	4.36
Control	20	2000	0.35	0.35	0.70	2.40	0.20	2.60
P			>0.05	>0.05	>0.05	<0.05	>0.05	<0.05

Table 2. Incidence of chromosomal aberrations and aneuploid cells in culture of peripheral blood leukocytes of subjects as a function of cumulative dose of external gamma radiation

Sub-group	Number of subjects	Cumulative radiation dose, mSv	Work tenure years	Aberrations (per 100 cells)		Structural aberrations (per 100 cells)	Cells (%) with		Total aneuploid cells, %
				chromosome	chromatid		44-45 chromosomes	47	
1	11	10-30	4-15	0.73	0.54	1.27	5.09	0.18	5.27
2	8	31-50	9-15	0.75	0.62	1.37	3.12	0.25	3.37
3	11	51-200	12-17	0.54	0.27	0.82	3.91	0.27	4.18

chromosomal aberrations. Several reports (St. Zhivkov et al.; A. V. Sevan'kayev et al.; Bocian et al.; Donev et al.; Popescu and Stefanescu, and others) have demonstrated a reliable increase in incidence of structural aberrations with radiation doses under 50 mSv per year and even with annual doses of less than 10 mSv (Donev et al.; Forni et al.; Visfeldt). Such complex aberrations were found as dicentric and ring chromosomes (Bocian and Ziemba-Zak; Donev et al.; al.; Visfeldt). It is difficult to explain such discrepancies. Perhaps there was inaccurate dosimetry or unrecorded acute irradiation against the background of chronic exposure to low doses of radiation.

Thus, with chronic exposure to gamma radiation in doses of less than 20 mSv/year, with cumulative dose of external gamma radiation of 10-200 mSv in 4-17 years, no changes were demonstrated in incidence of chromosome aberrations, as compared to the spontaneous level.

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CSO: 1840/189

EXPERIMENTAL VALIDATION OF USE OF SOME ISOTHIURONIUM DERIVATIVES AS  
RADIOPROTECTIVE COMPOUNDS

Moscow RADIOBIOLOGIYA in Russian Vol 21, No 4, Jul-Aug 81 (manuscript received  
11 Feb 80) pp 521-525

[Article by Zh. A. Goloshchapova, T. N. Tuzhilkova and L. I. Mizrakh]

[Text] Experiments on C57B1/6 mice and white rats demonstrated the rather high radioprotective efficacy of phosphorus-containing isothiuronium derivatives, which have a wide spectrum of therapeutic action when given via different routes, so that it is promising to continue with the study of these compounds.

It has now been shown that there are agents among isothiuronium derivatives that have rather high radioprotective activity [1-3]. We tested the radioprotective effects of 27 phosphorus-containing derivatives of S-alkylisothiuronium derivatives; among them were two compounds, S-ethylisothiuronium diethylphosphate (I) and S-ethylisothiuronium metaphosphate (II), which are not inferior to the well-known radioprotector, AET [aminoethylisothiuronium], in their radioprotective properties [4]. Preliminary administration of I and II resulted in survival of 70% of lethally irradiated animals. In order to find the optimum conditions for using compounds I and II, we tested their radioprotective properties as a function of radiation dose, amount of agent given, time and route of administration of the compounds and animal species; determination was made of the range of therapeutic activity [5] and protection index [6].

## Material and Methods

In our experiments, we used 1460 male C57B1/6 mice weighing 20-22 g and 1320 male albino rats weighing 200-220 g. The agents were given intraperitoneally and intramuscularly in the form of aqueous solutions. In our study of acute toxicity, we determined the doses corresponding to LD<sub>16</sub>, LD<sub>50</sub> and LD<sub>84</sub>. Radioprotective properties of isothiuronium derivatives I and II were tested with total-body exposure to  $\gamma$ -radiation once, in the range of lethal doses from LD<sub>16/30</sub> to LD<sub>95-99/30</sub> (154.8-258.0 mC/kg), at a dose rate of 0.43 mA/kg. The compounds were given 15, 30, 60 min and 3 h before irradiation in doses ranging from 1/32 LD<sub>16</sub> to 3/4 LD<sub>16</sub>. The experimental and control groups of animals were irradiated at the same time. The radiomodifying effect of the compounds was evaluated on the basis of the DMF (dose modification factor) and number of nuclear bone marrow cells.

The results were processed by the method of probit analysis as modified by Litchfield and Wilcoxon [7]. Protection index I was calculated with the formula:

$$I = \frac{LD_{50}}{ED_{50}} \left( 1 + \frac{a}{100} \right),$$

where  $a$  is the radioprotective effect, %;  $LD_{50}$  is the dose that is lethal to 50% of the animals and  $ED_{50}$  is the dosage that causes survival of 50% of the animals [6, 7].\*

## Results and Discussion

**Toxic properties:** Table 1 lists information about acute toxicity of I and II. We see that, when given intraperitoneally, agents I and II differ little in toxic dose level:  $LD_{50}$  constitutes 1.98 and 1.97 mM/kg, respectively, in the experiments with mice. Toxicity of the compounds is virtually the same for rats, not counting some decline thereof for I ( $LD_{50}$  2.2 mM/kg). When injected intramuscularly, the toxic properties of the agents are significantly diminished.  $LD_{50}$  for II when given intramuscularly to rats is almost twice the intraperitoneal dose; the toxicity of I depends less on the route of parenteral administration.

Table 1. Toxic and radioprotective properties of S-ethylisothiuronium diethylphosphate (I) and S-ethylisothiuronium metaphosphate (II) given intraperitoneally (i.p) and intramuscularly (i.m)

Compound	Toxic dose, $LD_{50}$ *			Lethal dose, $LD_{50/30}$ , mC/kg**			
	mice		rats	mice		rats	
	i.p	i.p	i.m	i.p	i.m	i.p	i.m
I	515 1,98	575 2,21	700 2,69	232,2 222,1÷242,5	221,9 213,4÷230,6	229,6 214,6÷245,6	219,3 208,7÷230,1
II	365 1,97	360 1,95	660 3,56	242,5 233,7÷249,5	230,9 220,8÷241,2	224,5 207,9÷243,3	216,7 205,4÷228,6
Control	—	—	—	203,8 196,1÷227,6	197,4 191,7÷203,3	194,8 181,6÷208,7	193,5 182,9÷206,9

\*Top line--toxicity, mg/kg; bottom line--mM/kg.

\*\*Agents given in a dosage of 0.4 mM/kg 15 min before irradiation.

Thus, the toxic doses of agents I and II are similar, so that we were able to study their radioprotective properties with the use of equimolar amounts. The

\*Translator's note: In the source, "SD" is used for "fatal dose" when referring to the drugs, but is rendered here as LD.



clinical signs of poisoning by isothiuronium and its phosphorus-containing derivatives, I and II, were similar: administrations of the compounds in a dosage of LD<sub>50</sub> elicited brief depression of general condition and motor activity, followed by motor excitement, clonic and tonic seizures and faster respiration after 10-15 min; death occurred within 30-40 min.

**Radioprotective properties:** Figure 1 illustrates the results of studying animal death as a function of radiation dose. Analysis of the dose-effect curves revealed that preventive administration of isothiuronium derivatives I and II prolonged substantially animal survival, in the case of exposure to both median lethal and sublethal doses of radiation, and the effect was the same as that of AET. Further increase in radiation dose beyond LD<sub>95/30</sub> (245.1-258 mC/kg) reduced the efficacy of the compounds drastically: after exposure to radiation in a dosage of 258 mC/kg, the survival rate was about 20% among animals "protected with I and II."

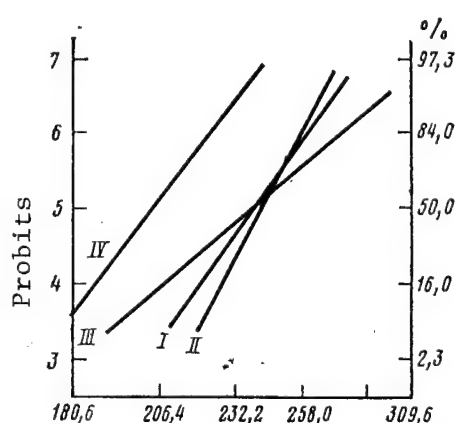


Figure 1.

30-Day survival of mice given isothiuronium derivatives intraperitoneally 15 min before irradiation as a function of radiation dose; X-axis, radiation dose, mC/kg; y-axes, mortality on the left and probits, %, on the right

- I) S-ethylisothiuronium diethylphosphate
- II) S-ethylisothiuronium metaphosphate
- III) AET
- IV) control

A comparison of the median lethal doses of radiation (Table 1) revealed that LD<sub>50/30</sub> increased by over 25.8 mC/kg with administration of I and II in equimolar amounts, as compared to the control, while the values of DMF constituted 1.14 and 1.19. Although the DMF is somewhat different for each of the compounds, these differences were statistically insignificant. A similar dependence of radioprotective effects of isothiuronium derivatives on radiation dose was also demonstrated with administration of the agents intramuscularly. A comparison of equieffective radiation doses revealed that, in this case, LD<sub>50/30</sub> increased by 24.5 mC/kg with administration of I and by 33.5 mC/kg with II. However, as was the case with intraperitoneal injection of the agents, the differences in their radioprotective activity were statistically unreliable. In the experiments on rats, the radioprotective properties of the compounds also showed little dependence on route of administration: compound I raised LD<sub>50/30</sub> by 33.5 mC/kg when given intraperitoneally and by 25.8 mC/kg when given intramuscularly, while compound II raised it by 29.7 and 23.2 mC/kg, respectively.

Thus, the mode of administration of compounds I and II had virtually no influence on their radioprotective efficacy. The correlation between median lethal doses in the experiment and control (DMF--Table 1) for compounds I and II given intraperitoneally to mice constituted 1.14 and 1.19; when given intramuscularly, it constituted 1.12 and 1.17. In the experiments on rats, DMF was 1.18 and 1.16 with intraperitoneal administration, 1.13 and 1.12 with intramuscular injection.

Table 2. Changes in LD<sub>16,50,84/30</sub> when agents are given to mice intraperitoneally (0.2 mM/kg) 15 min before irradiation

Compound	Lethal doses, mC/kg			DMF with LD <sub>50/30</sub>
	LD <sub>16/30</sub>	LD <sub>50/30</sub>	LD <sub>84/30</sub>	
I	223,2	232,2 219,0÷246,1	242,5	1,08
II	209,0	228,3 214,9÷242,5	250,3	1,07
Control	198,7	214,1 204,8÷223,7	221,9	—

Table 3. 30-Day survival (%) following  $\gamma$ -irradiation (232.2 mC/kg) as a function of dosage of chemical compound\*

Group	Agent	Dosage of agent, mM/kg						ED <sub>50</sub>		I
		0,05	0,1	0,2	0,4	0,8	1,2	mM/kg	mg/kg	
Mice**	I	—	10	10	60	40	100	0,4 0,33÷0,5	105 85÷130	7,4
	II	0	40	65	60	55	75	0,2 0,1÷0,3	40 31÷52	13,7
Rats***	I	0	10	40	40	60	—	0,4 0,3÷0,5	110 81÷148	9,5
	II	50	40	70	60	70	—	0,1 0,08÷0,14	20 15÷26	46,0

\*Survival rate in the control is 0%, number of animals in groups--10-20.

\*\*Agent given intraperitoneally 15 min before irradiation.

\*\*\*Agent given intramuscularly 15 min before irradiation.

A decrease to one-half of dosage of agents (0.2 mM/kg) reduced their radio-protective efficacy; DMF dropped from 1.14 to 1.08 for agent I and from 1.19 to 1.06 for agent II when given intramuscularly to mice (Table 2). In order to determine the range of therapeutic activity of I and II, experiments were conducted on animals, exposing them to radiation in a dosage of 232.2 mC/kg, giving the agents intraperitoneally and intramuscularly (Table 3). As we see, the survival rate increased with increase in dosage of the compounds. The wide range of doses we used enabled us to calculate for each of them the effective dose resulting in 50% animal survival (ED<sub>50</sub>). As can be seen in Tables 1 and 3, ED<sub>50</sub> differed substantially for both compounds from the median toxic doses (by 5 or more times) in the experiments on mice and rats.

We also studied the effect of time of administration of the products before irradiation. The agents were given intraperitoneally in equimolar amounts (0.4 mM/kg) 15 and 60 min prior to irradiation in doses of 154.8-232.2 mC/kg.

The results revealed that the radioprotective effect is significantly diminished when the interval between administration of the agents and irradiation is increased. Thus, when the compounds were given 15 min before irradiation, median lethal doses constituted 221.9, 230.9 and 197.4 mC/kg for I, II and the control, respectively, while DMF constituted 1.12 and 1.17 for agents I and II, respectively. LD<sub>50/30</sub> constituted 216.7, 214.1 and 205.1 mC/kg when the agents were given 1 h before irradiation for I, II and the control, respectively, while DMF constituted only 1.06 and 1.04. Similar data were obtained in the experiments where the effect was assessed according to quantity of remaining bone marrow cells 3 days after irradiation (Figure 2). As we see, the most cells survive when the products are given 15 min before the animals are exposed to radiation.

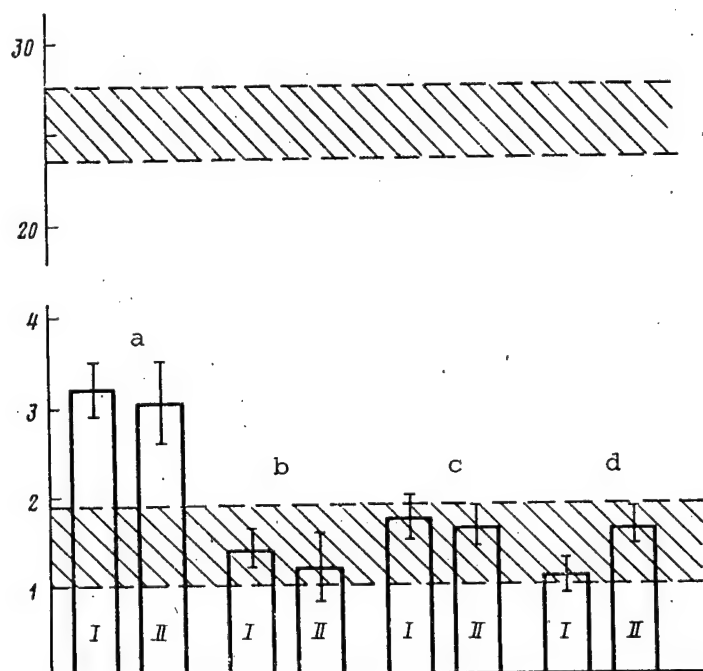


Figure 2. Bone marrow cells of mouse femur 3 days after exposure to radiation in lethal dose of 232.2 mC/kg when compounds I and II were given 15 min (a), 30 min (b), 60 min (c) and 3 h (d) before irradiation. Cross-hatched top band--biological control; bottom band--radiation control. Y-axis, quantity of bone marrow cells in mouse femur, millions

Thus, the results of extensive biological experiments to test the radioprotective efficacy of two derivatives of isothiuronium, S-ethylisothiuronium diethylphosphate and S-ethylisothiuronium metaphosphate, which differ only in phosphorus radical, revealed that both agents are moderately toxic and have radioprotective properties (DMF about 1.2) in experiments on two species of animals, when administered intraperitoneally and intramuscularly. The calculated protection index (Table 3) warrants classification of these compounds in the group of moderately effective (I) and effective (II) agents [6]. The foregoing is confirmed by the results of an additional experiment,

where we used 100 rats in each experimental and control group. The agents were given in equally effective doses--0.4 and 0.1 mM/kg for agents I and II, respectively. The radiation dosage was 232.2 mC/kg. The survival rate was 45% for experimental groups of animals, versus 10% in the control.

Thus, our studies revealed that the radioprotective properties of the tested compounds are demonstrable in different animal species with different routes of parenteral administration, and they were found to have a broad therapeutic effect. We had demonstrated previously [8] that agents I and II do not have a local irritating effect when given by the tested parenteral routes. This warrants consideration of phosphorus-containing isothiuronium derivatives (S-ethylisothiuronium diethylphosphate and S-ethylisothiuronium metaphosphate) as being worthy of further investigation.

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UDC: 615.357.63.015.2:615.849.1.015.23.076.9

COMBINED EFFECT OF HORMONES AND RADIOPROTECTIVE AGENTS ON ANIMALS EXPOSED  
TO IONIZING RADIATION

Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 2, Feb 82 pp 65-68

[Article by Gy. Benko, Lt Col Med Serv, candidate of medical sciences,  
K. Bodo-Sekeykhidine and A. Santha Col Med Serv (Ret), candidate of  
medical sciences (Hungarian People's Republic)]

[Text] Protein synthesis is inhibited and there is concurrent intensification of catabolism when an organism is exposed to ionizing radiation. Anabolic hormones, being specific enzyme activators, have a stimulating effect on protein synthesis and can retard its accelerated breakdown. Anabolic agents also have radioprotective properties.

Panek et al. (1972) studied total blood serum protein content after irradiation of animals given dianabol (methandrostenolone). Radiation doses of 450 and 650 R elicited gradual decrease in total protein content in animals that were not given this agent, with concurrent increase in activity of cathepsins of liver and kidney tissues; in those given the agent they led to insignificant impairment of protein content and slight increase in cathepsin activity. Other authors (I. N. Yefimov, 1968) reported that testosterone had a radioprotective effect.

According to the theory of Bacq (1961), the increase in cathepsin activity after radioactive irradiation is the result of damage to lysosomes, injury to the reservoir of enzymes of the hydrolase type and release of these enzymes. Disturbances in protein synthesis with the use of semilethal and lethal doses of ionizing radiation (Borhegyi et al., 1974) and the associated catabolic processes are attributed either to injury to the above-mentioned enzymes or other factors.

Of interest is the study of the combined effect of hormones with anabolic action and radioprotective compounds on irradiated animals. Danysz and Gronow et al. (1969) tested the combined effect of dianabol and cystamine. They obtained good results in animals given anabolic agents several days before irradiation, then cystamine. It was established that anabolics enhanced significantly the radioprotective effect of cystamine. With this in mind, we tested the combined effects of anabolic and other related therapeutic agents used in our country with radioprotective compounds that we had previously checked in experiments on animals (Santha et al., 1974).

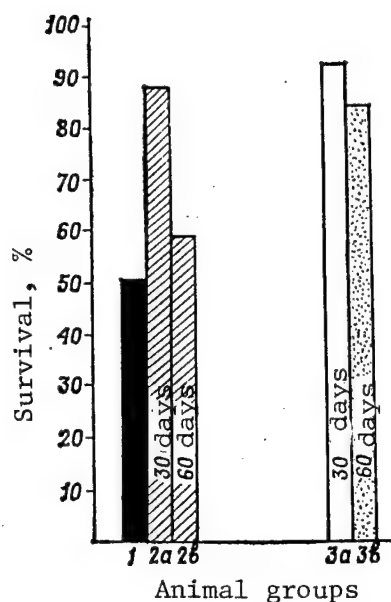


Figure 1.

Mouse survival on 30th and 60th days after exposure to LD<sub>50</sub> of gamma radiation with use of hormones

- 1) control
- 2) 750 R + 25 mg/kg retandrol
- 3) 750 R + 10 mg/kg nerobolil

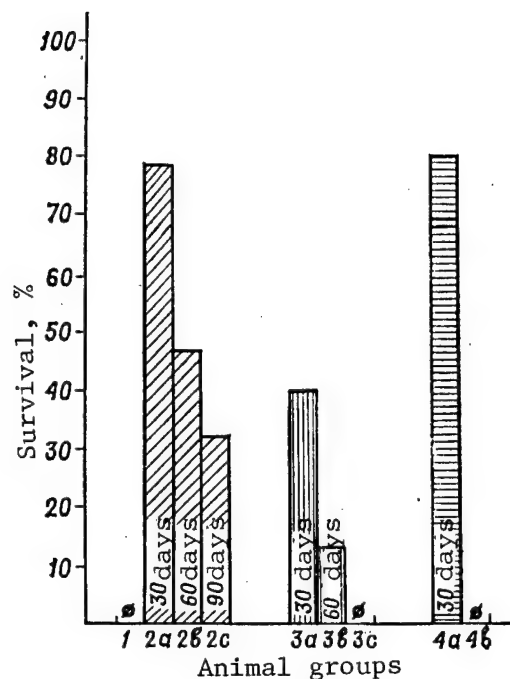


Figure 2.

Mouse survival on 30th, 60th and 90th days after 630 R x-radiation with use of hormones

- 1) control
- 2) 630 R + 10 mg/kg nerobolil
- 3) 630 R + 25 mg/kg retandrol
- 4) 630 R + 50 mg/kg retabolil

Studies were conducted on male albino CFLP (LATI, Godollo) mice. A THX-250 type unit for deep irradiation was used to deliver x-rays in doses of 630 and 800 R. The irradiation parameters were as follows: focus distance to middle of the body 60 cm, voltage 200 keV, filter 0.05 Cu, dose rate 44.4 R/min. For gamma irradiation, we used a unit with <sup>60</sup>Co source. A dosage of 800 R x-rays is considered absolutely lethal, 630 R is considered the minimum lethal dose, while 750 R gamma radiation corresponds to LD<sub>50</sub>.

The following radioprotective compounds were used: AET (S<sub>2</sub>-beta-aminoethylisothiuronium bromide-hydrobromide) and ikseprin (bis-alpha-propinyl-glycyl-disulfide sodium). The anabolic hormones we tested were retabolil (norandrosthenolone phenylpropionate) and retabolil (norandrosthenolone decanoate) produced by the Gedeon Richter Plant. We also tested retandrol (testosterone phenylpropionate), which is not an anabolic agent, but used in oncology for maintenance therapy.

We began to inject intraperitoneally nerobolil (10 mg/kg) dissolved in injection oil, retabolil (50 mg/kg) and retandrol (25 mg/kg) to groups of 15 mice 3 days before irradiation. The control groups were given only 0.5 ml oil intraperitoneally. In another series of experiments, the hormones were given after irradiation also. Radioprotective agents were usually given 20 min

before irradiation. Since ikseprin is an effective radioprotector even after exposure to ionizing radiation, it was given 3 h after irradiation.

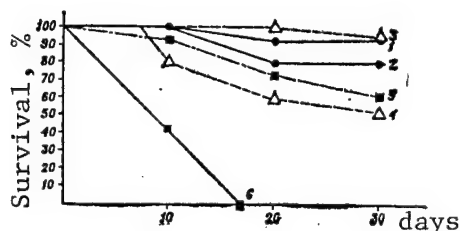


Figure 3.

Survival of animals exposed to lethal doses of x-radiation with use of AET before and hormones after irradiation

- 1) 280 mg/kg AET + 630 R + 25 mg/kg retandrol
- 2) 280 mg/kg AET + 800 R + 25 mg/kg retandrol
- 3) 280 mg/kg AET + 630 R + 10 mg/kg nerobolil
- 4) 280 mg/kg AET + 800 R + 10 mg/kg nerobolil
- 5) 280 mg/kg AET + 630 R + 50 mg/kg retabolil
- 6) 280 mg/kg AET + 800 R + 50 mg/kg retabolil

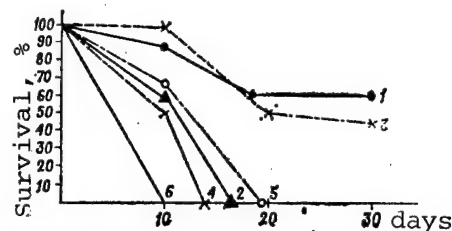


Figure 4.

Survival of animals exposed to lethal doses of x-radiation with use of ikseprin and hormones after irradiation

- 1) 630 R + 370 mg/kg ikseprin + 25 mg/kg retandrol
- 2) 800 R + 370 mg/kg ikseprin + 25 mg/kg retandrol
- 3) 630 R + 370 mg/kg ikseprin + 10 mg/kg nerobolil
- 4) 800 R + 370 mg/kg ikseprin + 10 mg/kg nerobolil
- 5) 630 R + 370 mg/kg ikseprin + 50 mg/kg retabolil
- 6) 800 R + 370 mg/kg ikseprin + 50 mg/kg retabolil

In assessing the results of the experiments, we took into consideration the number of animals that survived for 30 days after irradiation, as well as death rate. We also took into consideration weight gain of experimental animals.

Figure 1 shows that, after delivery of a 50% lethal dose of gamma radiation mouse survival rate constituted 90% under the influence of retandrol and nerobolil. The surviving animals were again exposed to LD<sub>50</sub> 30 days after repeated administration of hormones. Injection of retandrol on the 60th day provided 60% survival; with the use of nerobolil the figure reached about 85% (the entire control group died after the second irradiation).

On the 30th day after exposure to the minimum lethal dose of x-radiation, nerabolil and retabolil provided about 80% survival, whereas retandrol resulted in only 40% survival (Figure 2). After repeated administration of the agents and exposure to radiation, we demonstrated a substantial difference in the mechanism of action of these compounds, which are similar in structure. With nerobolil, animals that survived for 60 days constituted 48%, with retandrol the figure barely exceeded 10%; all of the mice given retabolil expired. After 3-fold irradiation and administration of nerobolil, we observed 32% survival; all of the animals expired with use of retandrol on the same program.

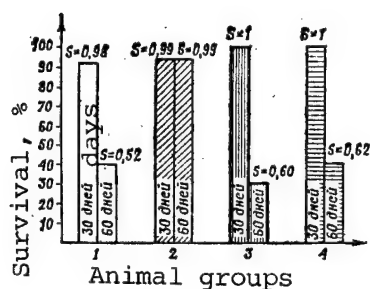


Figure 5.

Effects of hormones given before AET, as well as on 30th and 60th post-radiation days

- 1) AET + 630 R
- 2) retabolil + AET + 630 R + retabolil
- 3) nerobolil + AET + 630 R + nerobolil
- 4) retandrol + AET + 630 R + retandrol

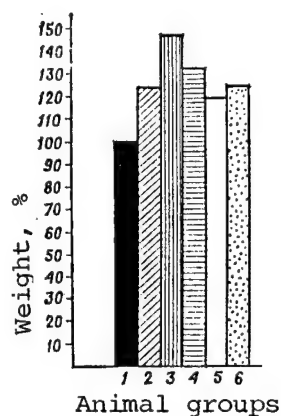


Figure 6.

Effects of hormones and radioprotective agents on weight gain by animals exposed to radiation

- 1) control
- 2) nerobolil + 630 R
- 3) nerobolil + AET + 630 R
- 4) nerobolil + ikseprin + 630 R
- 5) AET + 630 R
- 6) ikseprin + 630 R

We tested the effects of combinations of AET and the above-mentioned hormones with use of lethal doses of x-rays (630 and 800 R). Figure 3 shows how AET given before irradiation and single injections of hormones after exposure affected animal survival. Under these conditions, AET had a negligible effect, while retandrol and nerobolil elicited the maximum response.

We previously established that, unlike other radioprotective agents, ikseprin had a radioprotective effect when given after irradiation as well (Santha, 1974). We also tested its effect when combined with hormones. The results obtained under these conditions are illustrated in Figure 4. A radioprotective effect on animals exposed to radiation in a dose of 630 R was demonstrated only when ikseprin was combined with retandrol and nerobolil.

Figure 5 illustrates the results of testing the effects of hormones given before administration of radioprotective agent and after irradiation. Repeated injection of AET 30 days after x-irradiation (630 R) provided 40% survival. Combined use of AET and retabolil, which did not elicit a significant response on the 30th day as compared to AET alone (93-95%), had a beneficial effect when given a second time. With use of nerobolil after injection of a combination of nerobolil and AET on the 30th day survival constituted 100% (as with the combination with retandrol). In this figure, S refers to the coefficient of Kalusiner, which describes the rhythm of animal deaths (Logan, 1959). Using  $n$  to designate the number of post radiation days, we have:

$$S = \frac{n_1 + n_2 + n_3 + \dots + n_{30}}{n_1 \cdot 30}$$

The effects of hormones and radioprotective agents is also well-demonstrable according to weight gain by animals exposed to radiation (Figure 6).



Radioprotective agents (AET and ikseprin) elicited a 20-25% weight gain, which is essentially the same as the effect of nerobolil (24% weight gain). When animals were given a radioprotective agent before irradiation and nerobolil after, their weight increased even more.

Thus, single injection of anabolic combined with a radioprotector (AET or ikseprin) does not usually raise the survival rate of irradiated animals. According to our studies, combined use thereof is only effective when long-term administration of the anabolic follows preradiation use of the radioprotective agent. Best results were obtained with nerobolil. The beneficial effect of long-term administration of the hormone and radioprotective agent was also manifested by an increase in the animal's weight. When the hormone is given for a long time, death among surviving irradiated animals is reduced to a minimum when they are re-exposed to radiation.

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CSO: 1840/234

SURVIVAL OF DOGS EXPOSED TO LETHAL DOSES OF GAMMA RADIATION WITH USE OF  
CHEMICAL RADIOPROTECTIVE AGENTS FOLLOWED BY THERAPY

Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 2, Feb 82 pp 68-69

[Article by P. Kuna, docent, Lt Col, candidate of medical sciences and doctor of medicine, M. Dostal, docent, Lt Col, candidate of medical sciences and doctor of medicine, and P. Petyrek, Col, candidate of medical sciences and doctor of medicine (Czechoslovak Socialist Republic)]

[Text] The radioprotective efficacy of chemical compounds is studied extensively on small laboratory animals and, primarily on mice and rats exposed to total body radiation. There is a very limited number of studies testing the radioprotective properties of chemical protective agents on large animals, mainly dogs (A. S. Mozhukhin, F. Yu. Rachinskiy, 1979). In most studies, cystamine was given by intravenous injection.

A. S. Mozhukhin et al. (1965) gave cystamine dihydrochloride to dogs in a dosage of 60 mg/kg 30 min before x-irradiation. N. V. Butomo and V. I. Kuznetsov (1961) used this agent in a dosage of 50 mg base per kg animal weight in the form of 10% neutralized solution. T. V. Kavukchyan et al. (1974) used it in a dosage of 100 mg/kg 5 min before exposure to ionizing radiation. Radiation in a dosage of 200 R was repeated weekly to a cumulative dose of 800 R. The protective effect was associated with side-effects, which occurred immediately after the injection (salivation, vomiting, defecation, etc.).

In order to determine whether another parenteral route could be used to give chemical radioprotectors, we checked the efficacy of intramuscular injection of a combination of cystamine and mexamine in experiments on dogs (mongrels). We conducted experiments on animals of both sexes weighing 6 to 15 kg. The dogs were kept in wooden dog houses in an open paved area before and after irradiation. Series A of the experiments was conducted in the summer (June) and series B in the winter (February). Radiation was delivered without anesthetizing the dogs, but they were immobilized.

Gamma radiation in a dosage of 3 Gy (300 rad) was delivered to the estimated center of the animal's body (multilateral irradiation using a Chisobox radioactive cobalt source). The dose rate of the gamma field dropped from 1.169 to 1.053 Gy/min during the experiments.

Cystamine dihydrochloride, in a dosage of 50 mg/kg base or a combination of cystamine (24 mg/kg) and mexamine hydrochloride in a dosage of 4 mg/kg base

(combined double injection in the left and right gluteus maximus) was given intramuscularly 15-20 min before irradiating the animals. The chemical protective agents were dissolved in saline and injected in a volume of 0.4 ml/kg. Just prior to this, we gave an intramuscular injection of metoclopramide (Zerukal, GDR), an antiemetic agent, in a dosage of 0.5 mg/kg in order to minimize undesirable aftereffects. It did not prevent defecation after the injection of radioprotective agents in some dogs. Control animals were irradiated after giving them metoclopramide and saline.

Survival of dogs after exposure to gamma radiation with use of chemical protective agents followed by combined therapy

Series of experiments	Conditions of chemical protection and therapy	Number of animals	Sex	Survival	
				abs.	%
A	Saline IM [intramuscular]	8	4 F	2	25
			4 M		
	Therapy IM	8	5 F	6	75
			3 M		
	Cystamine+mexamine IM and therapy IM	8	5 F	7	87.5
			3 M		
B	Saline IM or IV (intravenous)	6	M	0	0
	Therapy IM	6	"	0	0
	Cystamine IV and therapy IM	6	"	2	33.3
	Cystamine IM and therapy IM	6	"	3	50

In previous experiments on purebred dogs (beagles), where there were 10 animals per group, only one of the control group survived by the 90th day after total-body multilateral gamma irradiation in a dosage of 3 Gy. In the group where preventive use was made of cystamine combined with mexamine after irradiation, three dogs survived. Four of the unprotected irradiated and treated dogs survived, whereas five survived after radioprotection before exposure and combined therapy after exposure were used.

In these experiments, systematic combined therapy was administered to all experimental irradiated dogs, with the exception of control animals. In essence, therapy consisted of repeated intramuscular injections of vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, B<sub>12</sub>, C, nicotinamide and calcium, pantothenate, vitamin K<sub>1</sub> and antibiotics--oxytetracycline and trimecaine, as well as gentamycin and streptomycin with procaine benzylpenicillin. Four injections of ferripolyglucin were given in the period from the 14th to 24th postradiation days.

We made various hematological and biochemical blood tests on the dogs before and after irradiation. Survival was assessed on the 90th or 45th postradiation days, and it was expressed as percentage of original number of experimental animals. We used the tables of Genes for statistical processing of obtained data.

The survival rates for irradiated dogs are listed in the Table, which shows that the efficacy of schematic combined therapy differed. In series A, we obtained (as before on beagles) a positive and reliable response to therapy

( $P = 0.01$ ). It was ineffective in the B series. A change in the environment and air temperature drop to minus  $6^{\circ}\text{C}$  had an adverse effect on the course of acute radiation sickness, and they apparently affected the severity of infectious complications and response to therapeutic measures.

Under such adverse conditions, there was an increase in importance of radioprotective agents for intensification of recovery processes. While we were unable to demonstrate a positive effect of chemical protection with post-radiation therapy in the experiments on beagles and those in series A on mongrel dogs, in series B the protective effect was distinctly manifested after both intravenous and intramuscular injection of cystamine.

T. V. Kavukchyan et al. (1974) report that necrosis and ulcers are produced if cystamine reaches tissues when injected intravenously. In order to determine the local effect of cystamine solution on muscle tissue, the appropriate tests were made in our laboratory. Preliminary results thereof revealed that, immediately after intramuscular injection, there is toxic damage to muscle cells, increased delivery of blood and reactive inflammation. These changes disappeared 3 days after the injection. Muscle reactions were also observed after injection of saline.

Blood leukocyte count dropped in all groups of equally irradiated dogs, regardless of use of chemical protectors or subsequent therapy. According to our data, it is impossible to give a prognosis of radiation sickness during the first week on the basis of the dynamics of changes in leukocyte count and other hematological or biochemical parameters.

Thus, repeated use of chemical radioprotective agents in the summer had no appreciable beneficial effect on rather successful combined therapy, which was administered for 28 days after exposure of animals to total-body gamma radiation. This therapy program was found, however, to be ineffective when ambient air temperature dropped to minus  $6^{\circ}\text{C}$ . Under these adverse conditions, the combination of chemical protective agents and subsequent therapy increased the number of surviving dogs after irradiation.

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CSO: 1840/234

ROLE OF  $\beta$ -ADRENERGIC RECEPTORS IN RADIOPROTECTIVE EFFECTS OF  
ISOPROTERENOL

Moscow RADIOBIOLOGIYA in Russian Vol 21, No 5, Sep-Oct 81  
(manuscript received 3 Jul 80) pp 688-693

GRAYEVSKIY, E. Ya. (deceased), SOBOLEV, A. S., SMIRNOVA, I. B., CHIRKOV, Yu.Yu.,  
DONTSOVA, G. V. and GRAYEVSKAYA, Ye. E., Institute of Developmental Biology  
imeni N. K. Kol'tsov, USSR Academy of Sciences, Moscow; Moscow State University  
imeni M. V. Lomonosov

[Abstract] Studies conducted with (CBA x C57Bl) $F_1$  mice demonstrate that subcutaneous administration of isoproterenol significantly enhanced 30 day survival rate (63%) following gamma-irradiation vis-a-vis untreated control or propranolol-treated mice (0%). Administration of propranolol jointly with isoproterenol abolished the protective effects of the latter. Studies on bone marrow tissue culture and addition of  $10^{-9}$  to  $10^{-4}$ M isoproterenol ( $\beta$ -adrenergic receptor agonist), propranolol ( $\beta$ -adrenergic receptor antagonist), or both, demonstrated that isoproterenol-mediated radioprotection consisted of two phases. During the initial 3 min of incubation radioprotective effects of isoproterenol and the rise in cAMP were abolished by propranolol, whereas addition of propranolol was ineffective after 12 min of incubation in terms of radioresistance and the rise in cAMP concentration. It appears, therefore, that early radioresistance is mediated by  $\beta$ -adrenergic mechanisms, whereas the late stages of radioprotection are primarily due to some other mechanisms responsible for maintaining high cAMP levels. Figures 3; references 11: 5 Russian, 6 Western.  
[147-12172]

BIOLOGICAL EFFECTS OF RADIATION IN CHRONIC HYPOXIA, PART 2: SPECIFIC AND NONSPECIFIC RESISTANCE IN RELATION TO ADAPTATION AND READAPTATION TIMES

Moscow RADIOBIOLOGIYA in Russian Vol 21, No 5, Sep-Oct 81  
(manuscript received 3 Apr 80) pp 694-698

GRIGOR'YEV, Yu. G., FARBER, Yu. V. and SHAFIRKIN, A. V.

[Abstract] Investigations were conducted on outbred male rats and male (CBA x C57Bl)F<sub>1</sub> mice to define the relationship between radio susceptibility and adaptation and readaptation times to high altitudes under pressure chamber or actual alpine conditions (both 3200 m). The results showed that increased tolerance of hypoxia was evident within 2-3 days of adaptation or readaptation; in the former case tolerance increased to three-fold the control level and remained elevated for the 30 day period of observation, while in the latter situation the initial three-fold increase in tolerance was replaced by a decrease to the control level which persisted for about 30 days. Radio-resistance, as a representative modality of nonspecific resistance, was seen to increase after about ten days of adaptation; afterwards it presented with harmonic fluctuations with a period of ca. 45 days and a maximum resistance about three-fold greater than the baseline resistance in primary adaptation. On readaptation a rapid three-fold increase in radioresistance was seen in ca. 3 days, which fell to baseline level in 4-6 days, rose again by day 30 and continued to fluctuate with a period of ca. 30 days. Both specific and nonspecific resistance were thus shown to be a function of the adaptation and readaptation time to prolonged hypoxia. Figures 2; references: 7 Russian. [147-12172]

UDC 577.391:577.3

STATISTICAL DESCRIPTION OF EFFECTS OF SINGLE HITS WITH HEAVY IONS OF BIOLOGICAL OBJECTS WITH NONUNIFORM GEOMETRY

Moscow RADIOBIOLOGIYA in Russian Vol 21, No 5, Sep-Oct 81  
(manuscript received 30 Jun 80) pp 756-761

KOVALEV, Ye. Ye., VIKHROV, A. I., NEVZGODINA, L. V. and SMIRNOVA, O. A.

[Abstract] A statistical study was undertaken to correlate the number of hits with charged heavy ions and the geometric nonuniformity of a biological object, using as a model *Artemia salina* eggs exposed to carbon nuclei (4.6 GeV/nucleon). The number of hits per egg was derived from the number of tracks made in a nuclear photoemulsion. There was agreement between the experimental observations and the proposed Poisson distribution for the number of hits at the 5%



significance level. This agreement indicated that a statistical approach can be utilized in the analysis of biological effects of high LET particles. Figures 3; references 7: 1 Western, 6 Russian.  
[147-12172]

UDC: 577.3:551:521.6

REACTION OF CULTURED BIENNIAL PLANTS TO VARIOUS TYPES OF RADIATION IN STAGES I AND II OF ORGANOCENESIS

Baku IZVESTIYA AKADEMII NAUK AZERBAYDZHANSKOY SSR: SERIYA BIOLOGICHESKIKH NAUK in Russian No 5, Sep-Oct 81 pp 117-121

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[Abstract] The purpose of this work was a comparative study of the reaction of culture biennials during the first year of life to various radiation exposures of the seeds and vegetating plants during various periods of ontogenesis. Studied were vegetables representing various families: carrots, beets and cabbage. The factors of influence were gamma, ultraviolet and infrared radiation. The criterion of response reaction consisted of the indices of initial growth processes, moist and dry mass of one plant at the end of vegetation. The results for all plants studied were similar. Gamma, UV and IR radiation of seeds and vegetating plants in relatively low doses caused no change or increased the plant mass. As dose increased the direction of action was reversed: the radiation began to have a depressing effect on plant growth. The phenomenon of nonspecificity of action of these factors cannot be made absolute, since any factor differs from others only in its inherent properties. Specificity is thus manifested primarily at the structurally fine levels of biological organization in the primary act of interaction of the factor with the matter. Figures 2; references: 14 Russian.  
[246-6508]

## PSYCHIATRY

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### COMBINED SOCIOTHERAPY OF MENTAL PATIENTS

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[Article by P. G. Derevyanchenko and L. I. Glukhova, Cherkasskaya Oblast Psychiatric Hospital No 1]

[Text] Although vocational therapy is the principal method of rehabilitation therapy, cultural therapy and group sports, as well as therapeutic physical culture occupy a significant place in it.

The forms of cultural therapy are diverse, and they depend on the objectives of the physicians in each specific case. They may consist of group viewing of telecasts, listening to the radio, reading and discussing newspapers, books, magazines, table games, participation in creative circles, cultural trips (to the movies, theaters), question and answer evenings, literary and musical gatherings, excursions to historical and noteworthy monuments in the city and oblast, etc. All this is feasible if there is the necessary material base (a club, library, radio broadcasting center, musical instruments, etc.).

Nurses specializing in cultural therapy, who are on the staff of each medical and diagnostic department and have undergone training on special programs under the supervision of a methodologist, organize the above-mentioned measures. They are highly qualified workers, enthusiastic about their work, capable of organizing and involving patients.

We have very interesting recreational evenings marking notable dates. For a long time, the patient retains a cheerful mood after spending 1.5-2 hours in the joyful atmosphere of such an evening. Contest winners are awarded commemorative souvenirs, which are often made by the patients themselves.

An individual approach is also required to prescribe therapeutic exercise for patients, as well as in conducting athletic events. At the first stage, we use two sets of therapeutic physical culture exercises with tonus-improving mode of exercise. They are conducted either individually or with specially formed groups. The program is gradually made more difficult, and the patient is transferred to an activating regimen. Athletics are also very beneficial to patients--individual or in sections (volleyball, basketball, table tennis, chess and checkers). These activities must have an element of competition, with naming of the winners, offering encouragement, broad announcement of

results to patients over closed-circuit ["local"] radio and on the bulletin boards, which the patients of each department produce.

Implementation of all of the above measures yields a positive effect; it is instrumental in calming mental patients, increasing their social and community activities, and ultimately affects the quality of treatment.

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